Postgraduate Medicine

UNIVERSITY
OF MICHIGAN
SEP 12 1950
MEDICAL
LIBRARY

Vol. 8, No. 2—AUGUST, 1950

ET—ADVANCES IN ALLERGY

Table of Contents on Pages A-5 and A-

"Few can afford to omit it from their libraries"

New!—FRIEDBERG'S DISEASES of the HEART

See SAUNDERS Advertisement on Pages 8 & 9

ertisement)

CRYSTOIDS® Anthelmintic is considered *drug of choice* for elimination of hookworm, roundworm and certain other intestinal parasites, because of its exceptional *effectiveness* and *safety*. A *single* administration is effective in 90% to 95% of cases of roundworm and 80% to 85% of cases of hookworm. Moreover, these parasites are usually killed outright, eliminating danger of migration.

CRYSTOIDS Anthelmintic pills contain crystalline hexylresorcinol, U.S.P. When properly administered (i.e., swallowed whole), CRYSTOIDS Anthelmintic pills are unusually free of toxicity.

CRYSTOIDS Anthelmintic pills are indicated in treatment of infestation with *hookworm*, *roundworm*, *pinworm* or *seatworm*, *whipworm* or *threadworm*, and *dwarf tapeworm*. Supplied in hard-coated pills of two strengths: 0.2 Gm. (package of 5 pills) for adults and children 6 years and over; 0.1 Gm. (package of 6 pills) for infants and children up to 6 years.

Sharp & Dohme, Philadelphia 1, Pa.

kills
hookworms,
roundworms
outright!

SHARP & DOHME

Crystoids®

anthelmintic pills

Repair of Tendon Injuries in the Hand

WITH SPECIAL REFERENCE TO FLEXOR TENDONS

R. GUY PULVERTAFT*

DERBY, ENGLAND

THE hand is constantly exposed to risk of injury from early childhood until the end of life. There is no lack of material for the surgeon whose interest lies in the hand. There can be few fields of surgical endeavor today where a new consciousness of our responsibility is more needed, both in treatment and in the organization of our accident departments.

All severely injured hands should be assessed by an experienced surgeon before treatment is commenced. It is not always possible to restore function to a severely damaged finger, and when tendon division is combined with severe skin loss or bone or joint damage, amputation may save unnecessary invalidism and stiffening of the remaining fingers.

Injuries involving the thumb or more than one digit demand a more conservative judgment, as even a portion of a finger may be of use to the mutilated hand.

The problems of late repair must also be considered in a critical spirit. It is unwise to attempt tendon reconstruction in the presence of severe scarring, trophic changes from digital nerve damage, or when the joints are stiff.

These complications must receive attention before tendon surgery is undertaken, otherwise the results will be consistently disappointing.

Tonight we are not concerned with the reconstruction of the hand ravaged by trauma or sepsis, but with the treatment of isolated tendon injuries. One of the foundations of successful reconstruction of the hand lies in the ability to deal with straightforward tendon division, and it is my intention to confine my remarks to this aspect of the problem.

*Surgical Director, Orthopedic and Accident Service, Derby; Surgeon, Harlow Wood Orthopedic Hospital; Civilian Orthopedic Specialist to the Royal Air Force. Derby, England.

Presented November 1, 1949, before the meeting of the Interstate Postgraduate Medical Association of North America, Philadelphia, Pennsylvania.

PHYSIOLOGY OF TENDON REPAIR

Synovial sheaths enclose those tendons which pass over joints and flex them through an angle. Tendons which slide in constant straight lines or which straighten joints from the forward flexed position are surrounded by paratenon, a loose, filmy connective tissue which contains elastic fibers.

Tendons held in apposition by external splintage or by internal suture heal in an orderly and progressive fashion. A fibroblastic reaction takes place in the tendon sheath or paratenon and glues the tendon ends together during the first week. Tendon cells grow out from the cut ends into this mass and the gap becomes bridged during the second week. This phase is characterized by the maximum vascularity of the tendons and the surrounding tissues. During the third week, resolution sets in and the tendon union becomes firmer until the junction takes on the appearance of normal tendon.

It is clear, therefore, that the process of repair

R. GUY PULVERTAFT

is associated with considerable reaction. This reactionary process subsides in due course, but if immobilization is continued for too long, firm adhesions develop which bind the tendon to its immediate surroundings.

This tendency to form adhesions is most marked in the digital theca, and the repair of flexor tendons or graft replacement in the fingers or thumb must be followed by very careful after-treatment.

Mason and Allen of Chicago have shown by experimental work that active movement commenced soon after suture results in an increased tissue reaction, whereas the tendon immobilized during the period of healing shows less irritative reaction and attachment to its surroundings.

It is not for me to criticize their work, and I know it is scientifically correct; I have met Mason and Allen, and I am a great admirer of their work. All I can say is that we can reach our goal in different ways, and in my personal clinical experience I have found that the better results after flexor tendon grafts have followed early commencement of active movements.

No reliance can be placed on the tendon union until well on in the fourth week, and if early movements are to be encouraged, the technic of suture and the materials used must be faultless, as the strain falls directly upon the suture material.

PRINCIPLES OF TREATMENT

It is not only useless but it is dangerous to undertake primary tendon repair unless certain fundamental conditions are satisfied.

1. The wound must have been caused by a reasonably clean instrument; a wound contaminated, for instance, by soil, I consider to be unsuitable for primary tendon surgery. Likewise, crush injuries are unsuitable for primary repair, as there may be necrosis of tissue beyond the limits detectable by the naked eye.

2. Cases complicated by skin loss and fracture or joint injuries are unsuitable for immediate repair.

3. Treatment must be instituted within a reasonable time of wounding. As you know, six hours is the generally accepted time for primary surgical closure, but this time can be extended and clinical judgment must dictate the final decision.

4. Operative conditions must be adequate and the correct instruments and suture materials available.

5. Tendon repair is precise work, and if the surgeon is not experienced in this type of work, the emergency operation should be limited to a careful wound cleansing and skin suture. Subsequent elective treatment may be carried out when wound healing is complete.

It is not difficult to suture tendons and prepare the ground for sound union. The real problem is to obtain a freely sliding tendon capable of restoring good function.

Extensor tendon divisions yield uniformly satisfactory results either by immediate or delayed suture, but flexor tendons, particularly when severed in the narrow digital theca, are likely to adhere to their surroundings if sutured in these areas.

Tendon junctions should be placed, if possible, where adhesions will not form so readily and where the tissues are more loosely arranged, as in the palm or forearm.

Immediate or delayed repair of the flexor profundus in the distal half of the finger will yield satisfactory results provided severe retraction has not occurred, but when both superficial and deep tendons are severed between the middle

finger crease and the distal palmar crease it is better to replace both tendons at a later operation by a single free graft which reaches from the terminal phalanx to a position well proximal in the hand. This graft with its own paratenon will constitute a new sliding assembly which is less likely to become adherent.

GENERAL TECHNIC

As I said, the restoration of function depends upon full joint mobility and a freely sliding tendon. The operative technic must therefore be designed to avoid any undue fibrosis. The tissues must be handled with the greatest care, and the most delicate instruments, such as are employed by ophthalmic surgeons, are used; all crushing of tissues and unnecessary interference with sliding surfaces is avoided. A bloodless field is, of course, insured by the use of a pneumatic tourniquet. Opinions differ a little as to how long the tourniquet may be safely maintained. It is my practice to regard one and a half to two hours as a safe period, and if the operation continues for longer than that, to release the tourniquet for five minutes.

The suture material should be fine but strong and of a nature which causes the least possible irritation to the tissues. We have found that stainless steel wire fulfills these requirements. It causes little or no reaction and provided kinking is avoided it is sufficiently strong in gauge 40 (0.0046 thickness of an inch) to permit guarded active movements before physiologic union has occurred.

The type of suture to be used depends upon the conditions present in each case, and there are three reliable methods in common use (Figure 1). First of all, the Bunnell-Mayer end-to-end stitch for joining two tendons of equal diameter; secondly, the Bunnell double right angle stitch used for a similar purpose but where there are several divided tendons as, for instance, at the wrist, that require rapid work; finally, the interlacing suture is used in those cases where the graft is much smaller than the accepting tendon. The diagram does not show adequately how the interlacing suture is performed. It is a difficult thing to draw. The graft passes through two tenotome slits at different levels and transverse wire sutures are inserted. Finally, in order to turn it into an end-to-end suture, the small tendon is drawn out through the end of the large tendon and it is enclosed somewhat in the manner shown.

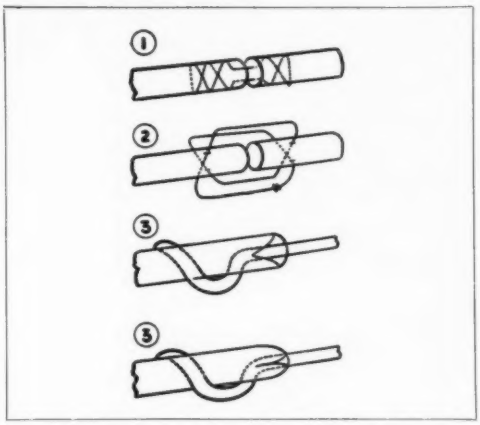


FIGURE 1. (1) Bunnell-Mayer end-to-end stitch. (2) Bunnell double right-angle stitch. (3) Stages in forming interlacing stitch.

The incisions are of great importance. They must be carefully planned to follow the natural skin lines and never should a flexion crease be crossed, as contractures and keloid formation will inevitably follow. I will talk a little later about the actual incisions that we have used.

Rapid progress may be expected after extensor tendon suture, but flexor tendon repairs and all the free graft procedures are followed by a gradual restoration of function and it is often nine to twelve months and sometimes even longer before the final result can be assessed.

TYPES OF FLEXOR TENDON REPAIR

I NOW propose to mention the various types of flexor tendon repair and make a few remarks about each variety. First of all are those divisions within the digital theca.

The profundus tendon—In cases of profundus tendon division or rupture, the choice of treatment must be guided by the main wound principles already pronounced. Immediate suture with stainless steel wire can give almost perfect results. Delayed suture is also satisfactory, provided the lapse of time has not been sufficiently long to allow severe retraction and secondary shortening of the muscle to occur.

If retraction renders direct union impossible, replacement by free graft should be considered, but this requires careful judgment. It is obviously unwise to perform a standard flexor graft, and

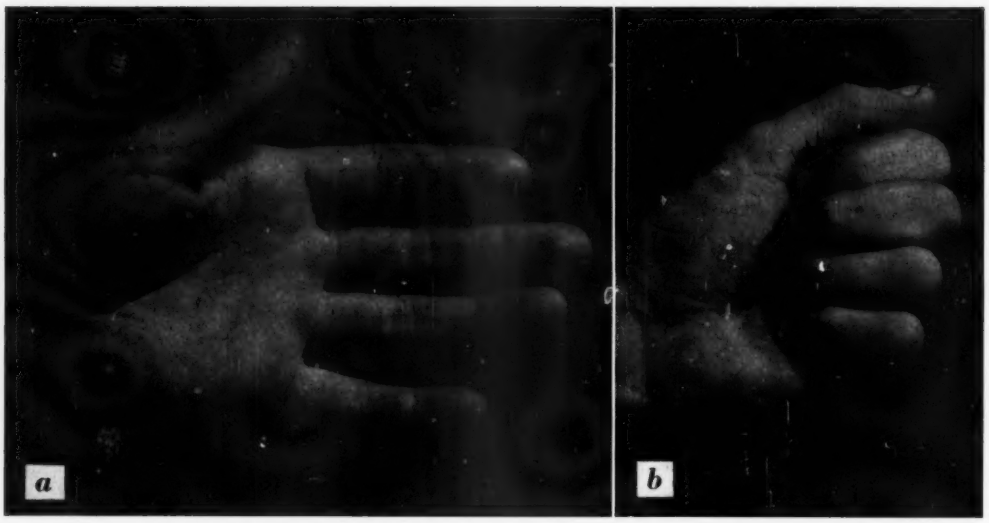


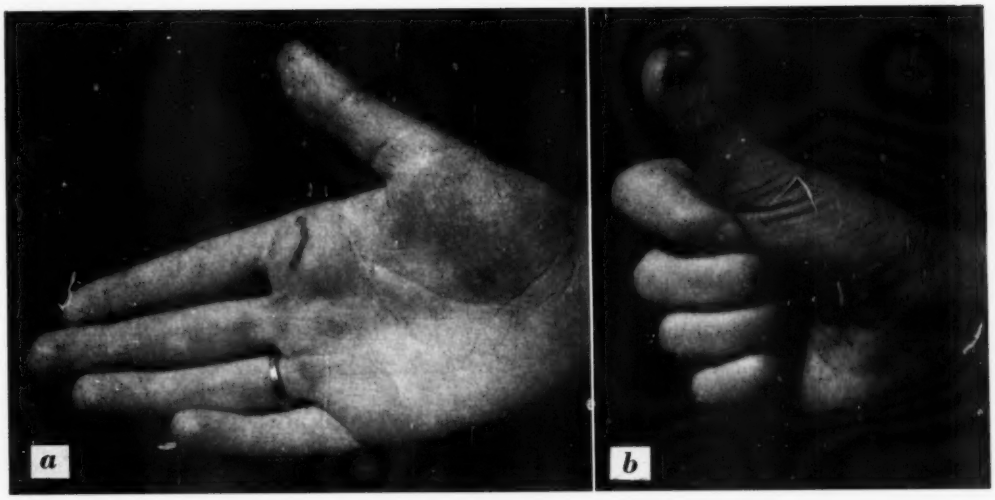
FIGURE 2 *(above)*. Division of both flexor tendons (middle, ring and little) at level of wrist. Also ulnar nerve and flexor carpi ulnaris. Immediate suture—tendons and nerve. (Wrist splinted six weeks—fingers immediate graded movement.) A. Extension. B. Flexion.

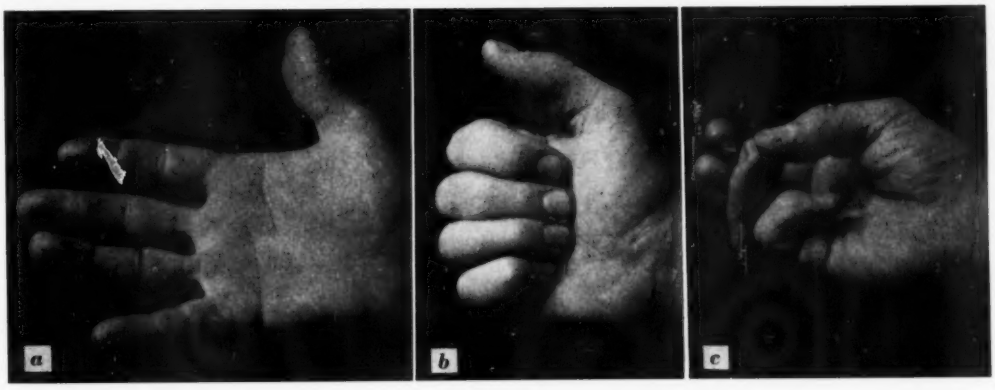
FIGURE 3 *(below)*. Division of the flexor tendons (index) at level of metacarpo-phalangeal joint. Previous immediate suture resulted in adhesions preventing movement. (No splintage—immediate strong movement.) A. Maximum flexion before tenolysis. B. Maximum flexion after tenolysis.

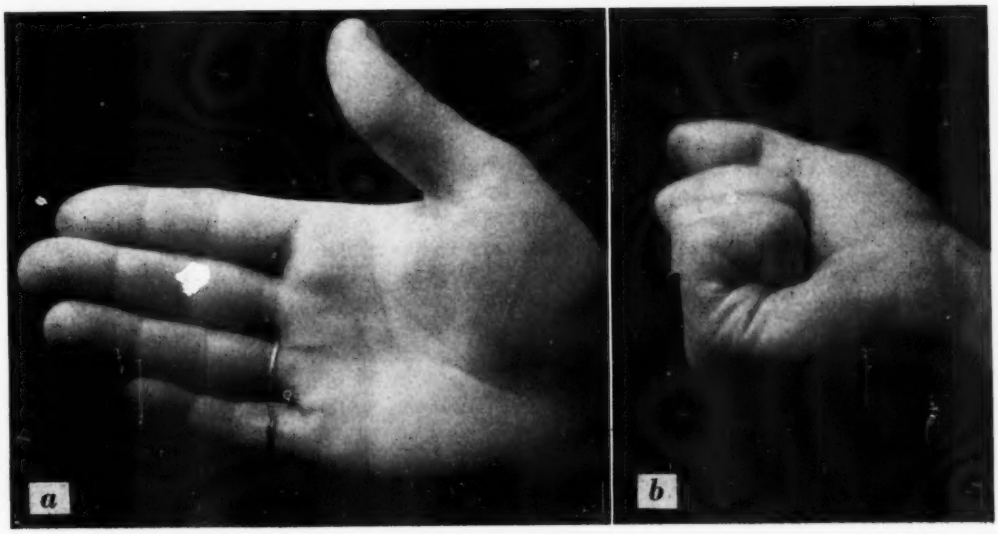
FIGURE 4 *(top)*. Division of both flexor tendons (index) at level of metacarpo-phalangeal joint. Replacement by palmaris graft and paratenon. (No splintage—immediate graded movement.) A. Extension. B. Flexion.

FIGURE 5 *(center)*. Division of both flexor tendons (ring) at level of proximal interphalangeal joint. Replacement by toe extensor graft and paratenon. (No splintage—immediate graded movement.) A. Extension. B. Flexion. C. Showing individual action of finger.

FIGURE 6 *(bottom)*. Division of both flexor tendons (little) at level of proximal phalanx. Replacement by palmaris graft and paratenon. (No splintage—immediate graded movement.) A. Extension. B. Flexion.







(Legends on opposite page)

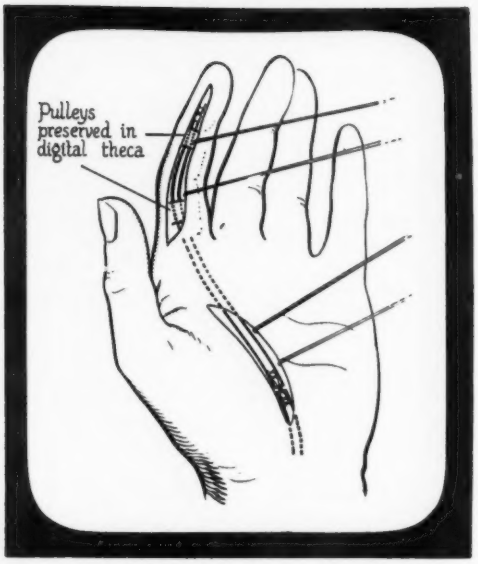


FIGURE 7. Tendon graft operation for flexor tendon division in digital theca.

(Figures 1 and 7 are reproduced from an article by the author published in Volume 6 of BRITISH SURGICAL PRACTICE, *by courtesy of Butterworth & Co., Ltd., Publishers, London.)*

in so doing remove a good functioning flexor sublimis. In order to restore the profundus we would thus run the risk of damaging the finger. Therefore, if a graft is to be employed, the sublimis should be left entirely alone and a thin toe extensor graft used to replace the profundus.

Combined profundus and sublimis division—This injury presents the most difficult single tendon problem in the hand and it is largely due to the work of Sterling Bunnell of San Francisco, Leo Mayer of New York, and Sumner Koch and Michael Mason of Chicago, that its treatment has been placed on a sound basis, and in England we invariably give credit to your great leaders.

I think it is only right to say that our knowledge—such knowledge as we have of this subject—is largely derived from the work that has been done in the United States.

The beautiful sliding action of the tendon in the digital theca makes one feel doubtful that restoration of function can ever be achieved by surgical treatment, but it has now been shown repeatedly that, provided correct principles and accurate methods are employed, excellent results can be obtained.

Site of the graft—There are several possible grafts available. Palmaris longus is the one most often employed and is present in approximately 90 per cent of subjects. It is of suitable size and length and can readily be removed. It should (and this applies to all taking of grafts) be taken with its surrounding paratenon by open dissection and not by using a tendon stripper.

Sublimis of the same finger may be used, but this tendon is sometimes found to be too thick, nor is it surrounded by paratenon.

We have for the past six years been using the long extensor tendons of the toes universally for tendon grafts. The extensor tendon of the second, third, fourth, or fifth toe may be used without harming the foot. These tendons are somewhat thin but appear to stand strain very well and by reason of their small size are readily revascularized. As I said before, the tendons are removed by open dissection and not by the use of a tendon stripper. There are other tendons that can be used in case of emergency, but I need not worry you about them.

Technic—The whole length of the finger is exposed by a true lateral incision which passes behind the digital vessels and nerves. The palm is exposed by an incision in the most suitable area. The sublimis and profundus tendons are completely removed except for a small tag of profundus attachment (Figure 7).

The channel between the finger and the palm is then stretched by Hegar's dilators and the graft is passed through two pulleys which are preserved in the original digital theca. The distal suture may be made either to the remaining tag of profundus or to the terminal phalanx.

One of the most important points of detail is the final tension. The tension should cause the finger to lie in the correct relationship to the other fingers while under the anesthesia, that is, the index finger flexed least and little finger flexed most. Suture lines should be secure and tested before final skin suture, because, as I have said, if we are to depend on early movements the suture must be secure.

In regard to after-treatment, I have tried various types, varying from splintage of the wrist in flexion for three weeks to no splintage at all, and I can say that for the last six years we have employed no splintage except in children and we have commenced movement the day after operation.

I would reiterate that the final result cannot be judged for nine to twelve months after operation, but in most cases the patient can safely return to useful employment in approximately six to eight weeks.

The thumb—Flexor pollicis longus can be sutured directly with a good prospect of success. Immediate or delayed suture should be undertaken according to the conditions of wounding. There are, however, some cases where suture is impracticable, owing either to the passage of time, severe retraction, or to marked scar formation. In these cases a free graft or one of the two following procedures may be used. Flexor pollicis longus may be elongated in the forearm by a slide at the musculotendinous junction and 1½ or 2 inches length gained in order to bring the tendon to the terminal phalanx. For those cases where both muscle and tendon have been destroyed, a complete muscle tendon replacement can be obtained by transferring a flexor sublimis unit, the complete unit, from a suitable finger to the thumb.

The palm—Tendon division in the palm does not present the difficulties encountered within the digital theca, and immediate or delayed suture can yield satisfactory results. Late cases in which retraction and lack of muscle elasticity prevent end-to-end suture may be restored by bridging the gap in profundus by a free graft taken from the sublimis, or by transferring flexor sublimis from a neighboring finger to the distal end of the divided profundus tendon.

Multiple tendon and nerve divisions at the wrist level—This presents a formidable surgical problem and opinion differs as to the correct precedence of nerve and tendon sutures. Nerve suture is technically easier and more satisfactory if it is delayed for several weeks after division. Tendon suture, on the other hand, gives far better results if it is done at once. If delay occurs, the tendon ends become glued into a mass and it is far more difficult to achieve good results. It was my practice to do both tendon and nerve division at the same time, but I have now followed the advice of Professor Seddon of London, who is our greatest exponent of peripheral nerve surgery, and he is convinced that the best results follow delayed nerve suture; so that the advice I would give is that tendons should be sutured at the wrist level at once and three to four weeks later you should be prepared to go in again and suture the nerve.

Finally, a very few words about tenolysis. The release of a tendon bound down by scar tissue resulting from trauma or infection is often followed by remarkable improvement in function. Passive joint mobility must be satisfactory, and in the case of postinfective adhesions the risks of awakening a dormant infection must be carefully weighed. The operation is tedious but not difficult. The tendon is completely cleared of all adhesions and a proximal exposure of the tendon or muscle is made in order to determine that a normal action is present before the operation is considered complete. I personally make no attempt to cover the tendon with glide material and place reliance entirely upon the after-treatment for the prevention of any further adhesions.

Immediate active movements are essential, and these, of course, can be strong because there is no danger of a suture line breaking down. The results are usually very satisfactory and at times dramatic in the speed and degree of recovery.

I would reiterate one point that I may not have stressed sufficiently. It is my belief that when both flexor tendons are divided between the middle finger crease and the distal palmar crease, no attempt should ever be made at primary or secondary suture, and all these cases should always be treated some weeks later by a free tendon transplant.

The present article is based on a Hunterian Lecture delivered to the Royal College of Surgeons of England in 1948. (By courtesy of the Royal College of Surgeons.)

CORRECTION

Dr. Rufus S. Reeves, author of the article, "Diagnosis and Treatment of Infectious Hepatitis" (*Postgraduate Medicine*, page 410, June, 1950), has requested the Editors to make the following correction relative to the use of Gamma Globulin (page 415): "The accepted dosage is 0.5 cc. per pound of body weight—rather than 2 cc. as stated."

Diagnostic Clinic

Periodic Fever and Periodic Abdominalgia

HOBART A. REIMANN*

JEFFERSON MEDICAL COLLEGE, PHILADELPHIA

My discussion concerns a new subject, although not necessarily a new disease, because it no doubt has been with us for many years but has been unrecognized as such.

The subject I have in mind is what I have called periodic disease and there have already been two publications covering the matter in the literature.

I have 2 patients to show you this morning. They represent respectively cases 1 and 2 of the published reports to which I just referred. Mrs. W., the first one, is the first patient I studied in this respect and she has been observed for some six or seven years. She is about 50 years of age. I think it best to discuss what the problem was when she was first seen by the physician who ultimately sent her to me. It was about 1941, when she complained of repeated attacks of malaise, fever, pains and aches, particularly in the flanks. Because the patient had had pyelitis in 1921 during a pregnancy, her physician naturally suspected pyelitis or pyelonephritis, because of the fever, chills, and pain in the abdomen and elsewhere.

She was studied intensively and had so many cystoscopies performed that it is surprising she did not develop pyelitis if she didn't already have it. Nevertheless, an intensive study was made, because it was thought that she had this type of infection.

*Professor of Medicine, Jefferson Medical College, Philadelphia, Pennsylvania.

Presented November 3, 1949, before the meeting of the Interstate Postgraduate Medical Association of North America, Philadelphia, Pennsylvania.

This went on for some time, and upon acquiring more history it was found that about thirteen years before, she had had spells of irritability, sweating, and mild aches and pains to which she did not pay very much attention. These did not discommode her very much until an emotional upset occurred, when these attacks became worse and sent her to the physician, as I just explained.

I first saw her in 1943 when the problem had not been solved. It was obviously not a case of pyelitis. These attacks such as she complained of between 1941 and 1943 consisted of irritability at first, general aching, fever, malaise, fever of 102 or 103° F. at times, nausea with vomiting at times, and pains generally, but especially in the extremities and in the abdomen, and particularly in the flanks.

This, of course, would have led to a long series of futile studies to discover the cause, and nobody up to that time had plotted the time relation of the episodes of discomfort which this patient has, which is the best way of discovering this type of disease. It has been my experience that a patient's memory so far as recalling the periodicity of attacks is unreliable. Some of them will say that they have attacks every two weeks, but if a record is kept the attacks will be found to come every month or every few days. You can easily realize how difficult it is to remember what went on last week or two weeks ago. The best thing to do is to make records on paper, which I will show you on the first slide.

Figure 1 covers a portion of an eleven-year record of Mrs. W.'s case and shows the average behavior of these attacks. It shows that these

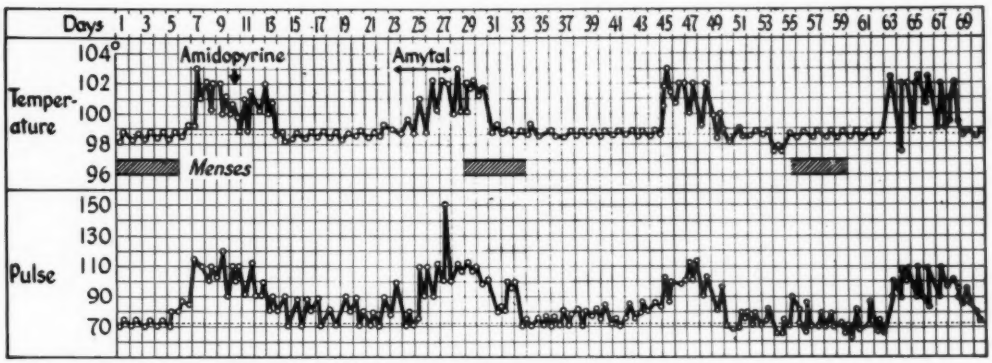


FIGURE 1. Portion of an eleven-year record of Mrs. W.'s case, showing average behavior of attacks of periodic fever and malaise.

attacks have no relation to the menstrual cycle. An episode starts with an abrupt rise of fever but it is preceded by a rise in the pulse rate. The attacks last four or five days, and between times she is normal, feels well, and of course keeps her position where she works. For economic reasons she has to keep her position during these attacks, in spite of feeling sick and, as she will tell you in just a minute, she is having one of these attacks at the present time.

This chart shows that the attacks recur at about twenty-one-day intervals.

During the seven years that I have been studying Mrs. W.'s case, all laboratory studies have been normal. I won't bore you with the numerous detailed studies we have made. Many physicians have seen her, including neurologists, psychiatrists, genitourinary surgeons, obstetricians, gynecologists, and others, in an attempt to discover the cause of these curiously regular episodes which she has.

At the present time she is in one of them; nevertheless, because she is obliged to work, she continues to work during these periods despite the discomfort entailed.

Mrs. W., your chief trouble is pain in the abdomen and extremities?

PATIENT: Yes.

DR. REIMANN: We measured her temperature a few minutes ago, and this morning it is a little over 99° F.; it may later rise to 103° F. In some episodes the fever is not of much consequence, but the pains in the abdomen and extremities go on just the same in varying degrees of severity and in varying combinations with the pains in the flanks and the chest.

The sedimentation rate is normal, as are all the other studies, except for occasional leukopenia. Because of the suggestion at one time that the episodes might be related to the menstrual periods, we made endocrinologic studies, but her excretion of estrogens, gonadotropins, and 17-ketosteroids was well within the normal ranges and there is no evidence that this patient's troubles are on an endocrinologic basis.

As you well know, in women there is a rhythmic temperature fluctuation synchronous with the menstrual period and apparently related thereto. It has been described as premenstrual fever. It has no relation to this type of fever which I am discussing.

The danger in these patients, of course, as you can readily understand, is that they are apt to be dismissed as neurotics because after years of study nothing abnormal can be found, except the temperature record. These patients are likely to go from doctor to doctor in the vain attempt to discover what the trouble is.

THE other patient who is here, Mr. L., represents case 2 in the published reports. He is about 30 years of age, is an accountant, and is greatly disturbed by repeated attacks of illness which do interfere with his work.

His trouble, like that of Mrs. W., began about twelve years ago when periodic attacks of headache, vomiting, and general discomfort came on about every month or two. In the course of time the intervals between attacks shortened, until now episodes recur approximately every seven days. For example, he can plan that every Mon-

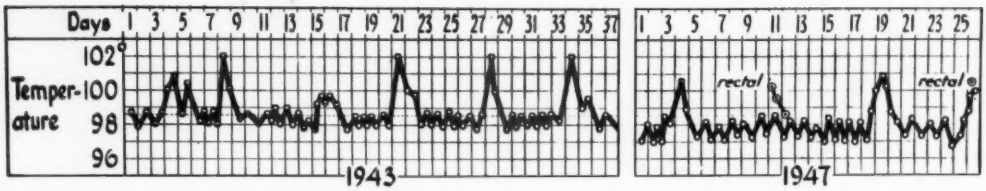


FIGURE 2. *(left)* Temperature record of part of hospital study of Mr. L. *(right)* Patient's own recording, under doctor's direction, done at home and at work. Periods of fever in both instances recurred at almost regular seven-day intervals.

day he will have a period of discomfort which is sometimes almost intolerable unless he controls his symptoms with acetylsalicylic acid, which permits him enough comfort to pursue his occupation.

These troubles begin with pain in the chest, shoulder, or abdomen, with headache, nausea, and fever. His temperature is not quite so high as Mrs. W.'s nor do the attacks last so long.

Before we saw him he had been subjected to the usual routine which so many doctors still persist in doing, futilely, of course, and that is searching for nonexistent foci of infection. As a result, he unnecessarily has lost a few teeth, his tonsils, and his appendix, all in an attempt to control the symptoms.

He explained his trouble to the Army induction officers in 1941, but they apparently did not pay attention to him, for he was inducted into the Army anyway, and you can guess what happened subsequently. He continued to have repeated attacks at weekly intervals and was an expense to the government in that he spent many months in various hospitals, in vain attempts to discover the cause of the trouble.

He spent six months in one hospital, and Figure 2 is a temperature record of part of that hospital study. Here again, during the eight- or nine-year period before I saw him, no one took the trouble to plot his episodes over a long period, or if they did they didn't pay any attention to the regular periodicity with which the attacks recurred. Figure 2 gives a clear picture of what can be learned simply by plotting the temperature and pulse rate.

The part of the temperature record on the left in Figure 2 was made at an Army hospital and, as you note, the bouts of fever occurred at approximately weekly intervals, not exactly, but it figures out to about seven days. The part of the chart to the right was the patient's own recording, under my direction, when he was at home and at work because he could not very well afford to spend time in the hospital where we wanted to study him intensively, except for the period in the middle where the rectal temperature was measured as illustrated by the lighter lines. Here again, as you see, the periods of fever recurred at almost regular seven-day intervals. The pulse rate also increases proportionately with the fever.

In his attacks, which occur with abdominal pain, it is obvious why appendicitis might be suspected because of fever, leukocytosis sometimes as high as 12,000 or 15,000, and pain in both lower quadrants. His appendix was taken out without any effect on the occurrences, which go on just the same now as they did before his operation.

In the diagnostic classification of these cases, it might be regarded as quibbling whether to regard Mrs. W.'s case as periodic fever and Mr. L.'s case as periodic abdominalgia because in Mrs. W.'s case there is abdominalgia and in Mr. L.'s case there is fever. I think, and I believe you will agree, that they are probably representative cases of the same syndrome or disease manifested by slightly different emphasis on different systems or symptoms. Mrs. W., for example, has fever as the most prominent manifestation, and in Mr. L.'s case the pain in the abdomen and other aches and pains are more prominent than the fever, so it is merely a question of choice as to the name used. Perhaps a better term would be not abdominalgia but visceralgia because of the aches and pains elsewhere.

Siegel reported several cases of this type and has called them benign paroxysmal peritonitis, which term I do not favor because there is no

evidence of peritonitis in my patients aside from fever and leukocytosis. Several of Siegel's patients also had been operated upon and only engorgement of the peritoneal vessels with some edema was found with no evidence of inflammation at all, so that I think the term visceralgia would be preferable. The term peritonitis unfortunately, in these patients, immediately suggests the need for sulfonamides and antibiotic therapy, which, of course, have no place whatever in the management of these cases.

These two conditions (if they are two separate conditions)—periodic fever and periodic abdominalgia—belong in a group of other periodic diseases which can be listed as periodic arthralgia, usually called intermittent hydroarthrosis, periodic or cyclic neutropenia, and the diseases called angioneurotic edema and Henoch's or Schönlein's purpura.

If one reads Osler's reports carefully, one finds throughout his descriptions of the latter two conditions that there is a regular periodicity in some of them. In one case of a family of five generations in which recurrent angioneurotic edema occurred as described by Osler, there was a man aged 92 who had had periodic attacks every two weeks since the age of 18. That means, of course, that he had attacks for seventy-four years and lived to the age of 92 with them. I rather hesitate to state that in view of this record my two patients have before them the possibility of suffering this discomfort for many years to come.

THE question is: What is the cause of these regularly recurring conditions? It is easy to set up an entity, but to discover the cause is another matter. There seems to be some common cause, and there have been several suggestions to account for it. One, of course, is allergy, which label we apply to so many things of which we know nothing, simply because it is a nice-sounding word and covers up a lot of ignorance. There are, to be sure, certain symptoms of an allergic reaction in many of these patients—not particularly in the 2 whom I cite here—which suggest to some that allergy does play a part. In studies that we have made, however, and those of others who have reported cases like it, we cannot incriminate any substance or group of substances as a cause of this curious condition.

Furthermore, it would be most unlikely that any allergen would produce symptoms as regularly as these patients have with exact time intervals over a period of twelve years in both of these patients, and, as I just mentioned, seventy-four years in the patient described by Osler.

Another suggestion is the operation of some endocrinologic disturbance because of the analogy perhaps with the menstrual period in women. But, as I have pointed out previously, there was no relation to the menstrual cycle in Mrs. W.'s instance or in any of the other cases which have thus far been described. Furthermore, these conditions often begin in infancy, sometimes as early as two months of age, and persist for life to old age. One would expect that there would be some endocrinologic change during these phases of life which would alter the regularity of the episodes. They also occur in men, in whom there is no evidence of an analogous menstrual-like cycle. So it appears that there is no obvious relationship to any of the endocrinologic functions. Furthermore, there is no evidence of known endocrine disturbance in any of the patients who have been described thus far.

The third possibility to consider is some infectious disease. Here again, as in the question of allergy, it would be most unlikely for any known infection to produce regularly recurring disease over periods of decades without any change in nature, without deterioration of the patient, or without ultimate recovery.

This brings us to the last suggestion, which is the best that I have to offer, hazardous as it may seem. It is that these reactions are the extreme manifestations of some natural rhythm of life to which we are all subject. Toynbee and several others have published books in which the rhythms of life are discussed, and suggest that all of nature is based on some rhythmic change. This explanation is the best I can suggest at the present time, and I let the matter rest here unless some of you have better suggestions to offer.

The immediate cause of these recurring conditions, as described here, I presume, is some vasomotor disturbance phenomenon which produces a transient edema of the areas from which symptoms arise and perhaps disturbs the heat-regulating center, but that is as far as I wish to speculate. Even if that were true it would not explain why these changes recur in regular cycles over so many years.

So far as the treatment of these conditions is concerned I think the most important thing is

to prevent a lot of the harm being done by removing a lot of detachable organs in an attempt to remove some nonexistent focus of infection.

The treatment is symptomatic. The patients themselves have usually discovered what helps them most. In Mr. L.'s case, the use of acetylsalicylic acid makes him fairly comfortable.

After my last paper was published, a doctor in New Hampshire wrote and told me that he had given one of his patients vitamin K and rutin on the assumption that some capillary permeability was responsible for the discomfort. Therefore, about a month ago I gave both of these patients rutin and vitamin K. They have taken the substances for only a month now, but without any change in the cycles.

The last suggestion would be to test the use of cortisone or ACTH, which seem to influence so many other diseases. We shall have to wait until these agents are a good deal cheaper and more plentiful. Periodic diseases are not serious ones except for discomfort, whereas cortisone and ACTH must be used at present in the more serious diseases such as rheumatoid arthritis, lupus erythematosus, and others.

I present these cases, then, as representatives of a newly recognized syndrome which it is important to know exists in order to protect these patients from a lot of unnecessary diagnostic procedures and, of course, unnecessary therapy.

BRAIN WAVES CONTROL ANESTHESIA DEVICE

(Photo, courtesy of American Medical Association)

The Servo-Anesthetizer, a new and revolutionary electronic machine, which makes it possible for a patient to administer his own anesthesia automatically during an operation, has been developed by the Mayo Clinic and was exhibited for the first time to physicians attending the 99th annual meeting of the American Medical Association in San Francisco.

The machine is the "brain child" of Dr. Reginald G. Bickford, former Royal Air Force medical officer, who joined the Mayo Clinic in 1946 as a research associate. He is now director of the electro-encephalography laboratory of the Mayo Foundation.

The device utilizes the principle that as anesthesia deepens, the energy output of the brain waves becomes less and less. A relay system, activated from the energy of the brain waves, controls the injection of the anesthetic agent into the vein or ether vaporizer. The brain waves can be viewed continuously on a small screen located in front of the machine or can be written on paper tape for permanent recording.

Diagnostic Clinic

The Management of Ulcerative Colitis

FRANK H. LAHEY*

THE LAHEY CLINIC, BOSTON

I AM particularly pleased to speak to you on the subject of ulcerative colitis because, up to the last few years, it has been an extremely depressing and crippling disease, one with a high mortality rate, and one in which the surgical procedures have been far from satisfactory. That picture has been entirely changed and it is now possible to rehabilitate these people completely by surgery so that, as I said, I am delighted to have the opportunity to speak to you about it and its complications.

TABLE 1
INDICATIONS FOR ILEOSTOMY

1. Acute fulminating cases
2. Medical failures
3. Massive hemorrhage
4. Subacute perforations, abscess, peritonitis, or fistulas
5. Obstruction
6. Polyposis
7. Malignant degeneration
8. Joint infection
9. Incontinence from rigid anus

The indications for ileostomy are listed in Table 1—the acute fulminating cases, the medical failures, the massive hemorrhages, subacute perforations, obstruction, polyposis, malignant degeneration, joint infection, and incontinence from rigid anus. The incidence of malignancy in ulcerative colitis has been all too little appreciated and only now the seriousness of malignancy in a patient with this inflammatory lesion of the colon is being realized.

I should like to stress in this list the problem of incontinence caused by the fibrosis and infiltration that often occur in the lower end of the rectum and the sphincter.

I should also like to add to the indications the multiple anal fistulas that not infrequently occur in the presence of ulcerative colitis. In 80 per cent of all patients with ulcerative colitis, the rectum and anal canal are involved.

In approximately 800 cases of ulcerative colitis seen at the clinic not all of the patients have required surgery. Many have been handled quite satisfactorily by medical measures. In a survey of our cases in which 327 were followed from two to fifteen years, it was found that medical management brought about either marked improvement or complete relief of symptoms in two-thirds of the patients with the milder forms and in one-third of those with the more severe forms of the disease. On the other hand, our changing concept of the relationship of malignancy to ulcerative colitis raises at least some doubt as to the wisdom of continuing medical management. We have been very well satisfied with medical management in most cases and if we did not have this new information troubling us about the increasing incidence of malignant disease in patients who have ulcerative colitis over a period of years, then we would still be satisfied to have a majority of the patients with ulcerative colitis treated medically, and I shall speak of that later.

*Director, Lahey Clinic; Surgeon, New England Deaconess Hospital; Surgeon-in-Chief, New England Baptist Hospital, Boston, Massachusetts.

Presented November 2, 1949, before the meeting of the Interstate Postgraduate Medical Association of North America, Philadelphia, Pennsylvania.

FRANK H. LAHEY

TABLE 2
SURGICAL TREATMENT OF ULCERATIVE COLITIS

	TO 1947	1947-1949	TOTAL
Number of patients operated on	166	97	263
Number of operative procedures	313	218	531
Ileostomy	145	70	215
Partial colectomy	46	9	55
Total colectomy	75	73	148

As to the data concerning the surgical treatment, it is of interest to note that we have divided our experience with these patients surgically into the group to 1947 and a group from 1947 to 1949 (Table 2). You will note that 263 patients have been operated upon, and the number of operative procedures has been 531. Up to 1947, 145 ileostomies were done and from 1947 to 1949, 70 ileostomies were performed. This division into two groups is of great value because it permits us to compare mortality, to compare the number of people who committed suicide in the first group and in the second group, and it permits us to compare the management of patients with ileostomy before we had the various ileostomy bags we now have.

THE 145 ileostomies in the first group play a great part in the changing concept of management of ulcerative colitis, because in this first group, up to 1947, 3 patients committed suicide. The mortality was 22.3 per cent. In the second group, no patients even thought of suicide, and the mortality was 4.1 per cent. Because of our better management generally, better management of the ileostomy with bags and ability to perform it with greater success, these patients should no longer be denied ileostomy when the indications are present as listed in Table 1.

You will note (Table 2) that there have been, in the first group, 46 partial colectomies and 9 in the second group; 75 total colectomies in the first group and 73 total colectomies in the second group.

It seemed to me it would be of great value to state the mortality figures (Table 3) before we discuss these problems, because you can see that real progress has been made in the surgical management of ulcerative colitis. It was the high mortality rate and the very unfortunate condition following ileostomy that prevented internists and gastroenterologists from sending these patients to surgery early enough so that the mortality could be kept down. Up to 1947 the patient mortality was 22.3 per cent, the operative mortality 11.8 per cent, but that has now dropped to 4.1 per cent and 1.8 per cent respectively.

Four deaths occurred in 1947 and 1948, 2 following ileostomy and 2 following ileostomy with right colectomy.

TABLE 3
SURGICAL MORTALITY IN ULCERATIVE COLITIS

	TO 1947	1947-1949
Patient mortality, per cent	22.3	4.1
Operative mortality, per cent	11.8	1.8
Number of deaths in 1947 and 1948		4
Following ileostomy		2
Following ileostomy with right colectomy		2

I would like again to place in your minds the type of segmental ulcerative colitis in which the lesion is limited to the rectum and the descending colon (Figures 1 and 2). It is in this type, I believe, that in most of the cases an ileostomy can be replaced with a colostomy if the resection and abdominosacral procedure are done early enough so that the lesion has not spread. If you see this same segmental lesion on the right side, you then have an opportunity to do

FIGURE 1. In this illustration may be seen segmental ulcerative colitis involving the rectum, sigmoid, and part of the descending colon. It is in this type, if the disease is definitely segmental, that a colostomy may be established in place of an ileostomy.

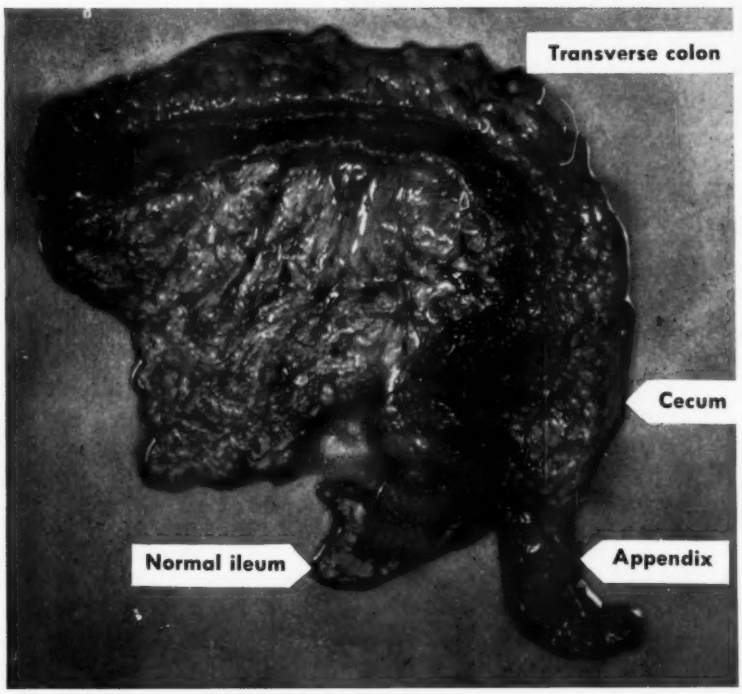


FIGURE 2. The actual specimen of a lesion of the type shown in Figure 2.

a wide resection and anastomosis of the ileum to the descending colon. We would strongly urge that no medical management delay the approach to surgery in this type of case, because never again will you have the opportunity to get rid of the entire disease and restore the fecal stream. This disease spreads along the bowel wall progressively; when it is a segmental lesion it tends to involve the rest of the colon, and not only does it spread over the colon but it spreads onto the terminal ileum and produces a type of terminal ileitis.

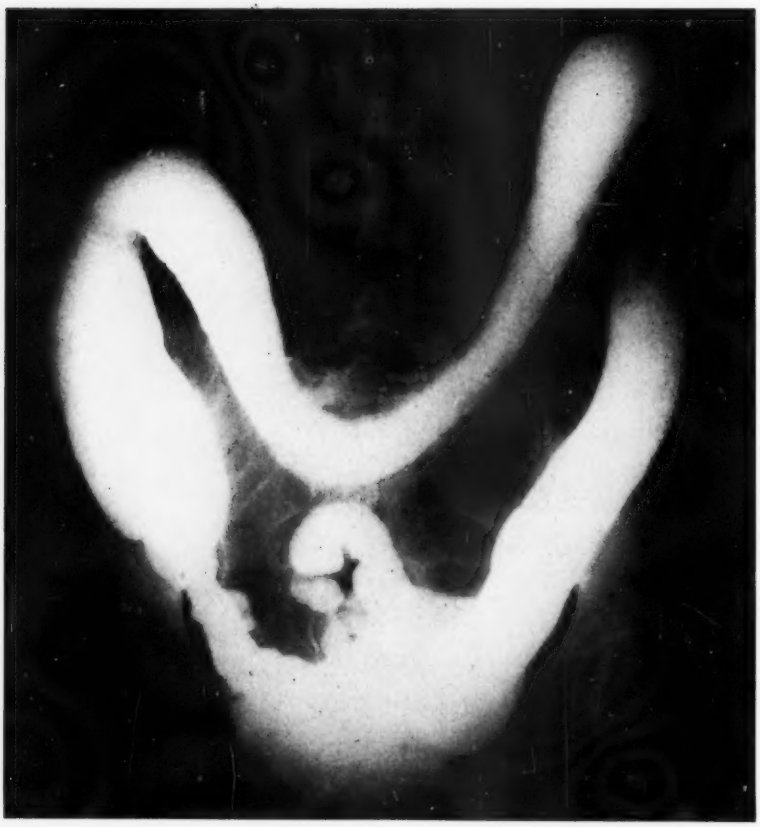


FIGURE 3. A typical lead-pipe colon, with complete absence of haustrations, is shown. Note the tendency to abolish flexures and the complete rigidity of the entire colon.

We have reported on our experience with this disease and with regional ileitis, that regional ileitis spreads over onto the colon and can produce an ulcerative colitis involving all of the colon, and in the reverse way ulcerative colitis can involve the terminal ileum and produce a terminal ileitis.

I WANT to show you the two types of lesions, to illustrate why colectomies should be done. The so-called lead-pipe colon is shown in Figure 3. The polyposis in the descending colon may be seen in Figures 4 and 5. Another thing that all surgeons have recognized in ulcerative colitis can be seen in the illustrations, and that is that the cicatrizing effect of ulcerative colitis abolishes the hepatic, the sigmoid, and the splenic flexures. When these colons are removed after they have existed as the lead-pipe type of colon, they are often not over 2 or 3 feet long. That is of importance because if a stage operation is to be done in colectomy and, for instance, the descending colon is implanted in the abdominal wall after the proximal ascending colon has been removed, very much more colon must be placed outside the abdominal wall for the three-month interval between the first and second stages, because the exteriorized part will cicatrize and withdraw within the abdomen.

In Figure 3 is shown the typical lead-pipe colon. These specimens are shown to urge that once an ileostomy is established with this type of colon there is no advantage in not doing the colectomy and the abdominosacral procedure.

When one sees the type of ulcerative colitis shown in Figure 4 with the polypoid degeneration, it is our opinion that this is an advanced stage of polypoid degeneration which increases materially the hazard of malignant degenera-

FIGURE 4. Another type of lead-pipe colon is shown in which the polypoid type of degeneration is evident, particularly in the region of the splenic flexure and descending colon. Note again in this cicatrized colon the gradual disappearance of the splenic and hepatic flexures by shortening.

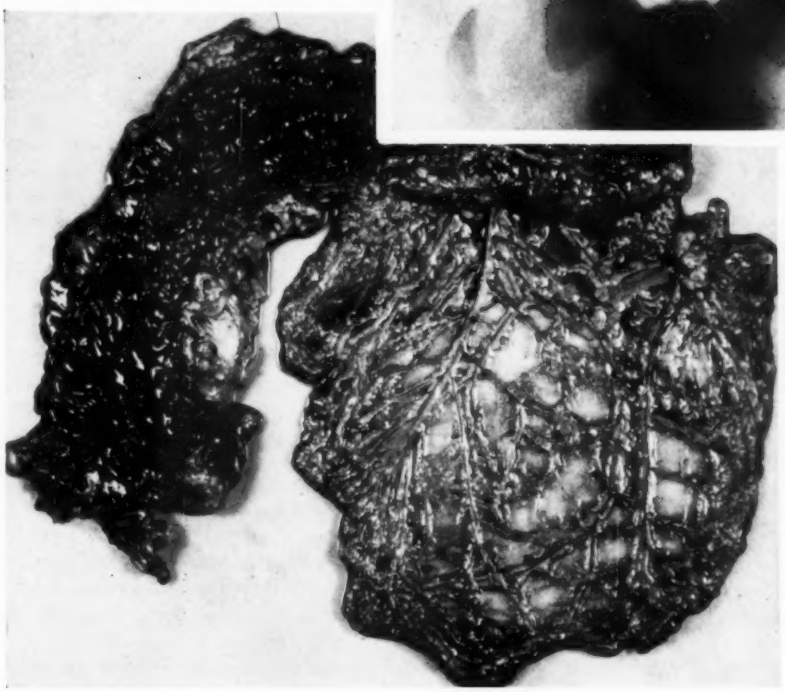


FIGURE 5. The actual specimen, showing polypoid degeneration as demonstrated in Figure 4.

tion and that there should not be any delay in its removal by colectomy and an abdominosacral procedure.

Having established the background of the disease from which to draw conclusions, I would now like to say something about how we should handle these patients from a surgical point of view. The greatest mistake that has been made and is still being made in the management of ulcerative colitis with complications

is delay; this delay is largely due to the fact that a great many general practitioners and internists are not aware of the fact that the Koenig-Rutzen bag and various other types of bags made for ileostomies so completely rehabilitate these patients.

These ileostomy bags are literally tailored to the ileostomy. They have an aperture which fits the ileostomy in such a way that no skin is exposed to become irritated. They are flat. They are made like a hot-water bottle and have a spigot at the bottom which can be folded over so that these patients can go to the toilet and empty the bag of its contents without detaching it from the abdominal wall. They are so flat that at a recent meeting of the National Gastroenterological Society I showed a young woman who is a professor of English in a college near Boston, who could wear a very tight-fitting dress or bathing suit, to demonstrate that the bag in no way disfigures the abdominal outline or makes it impossible for the patient to wear the same kind of clothes anyone else wears. These bags are completely water-tight. They can be worn swimming and one can do everything with them. For that reason I would strongly urge that, in the presence of complications, no longer should patients with ulcerative colitis come to surgeons with high temperatures, 14 to 16 bowel movements a day, with the jaundice of hepatitis, a distended abdomen, and in such a toxic state that an ileostomy can be done then only with the greatest hazard. This is what has caused the large mortality in the past in patients having ileostomies.

Whenever medical management fails to control the disease in these patients, they should, I believe, immediately have early ileostomy, which can be done deliberately and safely and without the hazards which used to go with the late ileostomies of the past.

It has been said that hemorrhage is not a serious complication of ulcerative colitis. It certainly is with us. We live in a thickly populated community where patients who bleed profusely from ulcerative colitis, as they not infrequently do, can be dumped in our laps for emergency management. In general we would not want to do ileostomies and colectomies on patients with ulcerative colitis in the presence of hemorrhage, but we are not infrequently compelled to, and must occasionally do emergency colectomies in the presence of massive recurring hemorrhages or lose the patients. There is almost no hemorrhage in a patient with ulcerative colitis too serious to make it necessary to advise against colectomies in these patients, and in some of the recurring hemorrhages it is the only way by which these patients' lives can be saved.

I HAD said up to the past year that never in our lives had we done a total colectomy and a combined abdominosacral removal of an ulcerative colitis in one stage, but last year I was forced to do it in a patient who had massive recurring hemorrhage with all of the colon and rectum bleeding. If it can be demonstrated that the lesion is in the descending colon, as evidenced by bright blood, and if bleeding is not controllable, then ileostomy followed promptly by the removal of the segment of colon is, and has been in our hands, a justifiable and satisfactory procedure. When, however, the disease involves all of the large bowel, total colectomy may be required.

What are the dangers of malignancy? Can a diagnosis of this lesion in patients with ulcerative colitis be made early enough and, if so, can these patients' lives be saved? We have had 18 cases of cancer of the colon in patients with ulcerative colitis and only 2 of these are now alive and they for only three years. In addition, in both of these cases the diagnosis was made on microscopic examination, being found by the pathologist at the time he examined the specimen.

It is unfortunate that the diagnosis of malignancy in ulcerative colitis cannot be made except in the presence of the three following conditions: (1) when there has been no bleeding and there is suddenly the passage of bright blood, (2) when there has been no obstruction and there is sudden obstruction, and (3) when there is a palpable mass, a superimposed malignancy can be suspected. But at all three of these stages it often is too late because the malignancy has occurred in the most disastrous site in which it can occur, and that is in the presence of an inflamed bowel.

When we realize that the general incidence of malignancy in ulcerative colitis is in the neighborhood of 5 per cent and that it increases with every year that that colon is left in, until it approaches 30 per cent in the patients who have had ulcerative colitis with their colon intact ten years, some doubt is raised as to the wisdom of permitting these patients who can

be treated medically to go on with this hazard of malignancy in a colon which is retained.

I would have agreed to this position, that is to retain the colon and a colostomy or ileostomy when this was followed by relief of all symptoms up to the time when it was possible to obtain such complete rehabilitation of these patients by means of the present ileostomies and their management with the newer ileostomy bags. Now we can restore these female patients so completely that they can even have babies. That has been an interesting development, because in so many of the patients with ulcerative colitis the women are young and when a complete dissection of the pelvis was done and the ileum attached to the abdominal wall, we have hesitated to permit these young women to marry and have babies. We have not had anything to say, however. They have asked us whether or not they could marry. We have said "no" and they have gone out and done it. We have now had enough of them get married and have babies so that we lean toward the position that if they have had their colons and rectums out, provided they and their husbands and their obstetricians recognize the added risk and it is not too great, they can be told that, with a reasonable risk, they can marry and have children.

One thing I would particularly like to call attention to and that is I do not believe that the average person who sees only occasional cases of ulcerative colitis is aware of the high incidence of joint destruction which is associated with this disease. Arthritis secondary to joint infection as a result of the infected material within the colon is a common complication of ulcerative colitis, much more common than many people realize. Here, I believe, an important point should be made. If you wait in these patients with joint involvement until the cartilaginous surfaces are destroyed, even though the infecting agent is done away with, complete joint function will never be restored by the colectomy. Joint involvement in patients with ulcerative colitis is an indication for immediate and early ileostomy and colectomy. If, with this complication, you delay too long you may regret it because joint motion cannot then be restored by removing the source of infection.

Another thing that has repeatedly been forced upon our attention is the inability of these patients with rigid sphincters and rigid rectums to remain continent. No patient with the multiple fistulas frequently associated with long-standing ulcerative colitis or with rectal incontinence should have to continue to suffer this way when his colon can so safely and satisfactorily be removed and a completely controllable ileostomy established that will not leak or smell.

Should we take the position that every patient who has had an ileostomy should have a colectomy and an abdominosacral removal of the rectum? I believe so, with firm conviction, and for these reasons. In patients with the indications listed in Table 1 we used to do ileostomies and leave the colon in if the patient did not have symptoms from it. A great many of these patients do have symptoms, a great many get joint infection and, in addition, there is, as I have already stated, the greatly added hazard of malignancy in these retained colons.

Another thing which I think is extremely important and interesting from a physiologic point of view, and from the point of view of the patient's comfort, is that the discharge from an ileostomy with the colon left in, even though the colon be largely destroyed, is entirely liquid and remains so in most of the cases. As soon as the colon is removed, however, in most of the cases the discharge becomes semisolid and much more easily controlled. When we look back on what is to be lost and what is to be gained in the patients who have ileostomies and compare those who have their colons out with those who do not have their colons out, there is much more to be lost by keeping the colon and much more to be gained by taking it out.

Regarding ileostomy, I would like to add one other thing, and that is that it is now possible to establish trial ileostomies. If these patients come at an early stage of their ulcerative colitis and, under good medical management, they do not obtain complete relief of symptoms in the way of cessation of the passage of blood, multiple stools, and lowered temperatures, a trial ileostomy can be done. We have done temporary ileostomies in 25 cases. Their colons are put completely at rest, and under the following conditions their fecal stream can be re-established. After the patient has had an ileostomy for a year, if he is completely relieved of all symptoms, if haustrations return within the colon as shown by x-ray examination, if on proctoscopic examination the rectal mucosa is normal, soft and velvety and not granular, and if—and this is extremely important—in addition,

the patient and his family have been told that in spite of all these things, restoring the fecal stream may awaken the disease and require another ileostomy, then, we believe, the fecal stream can be reestablished. We have restored the fecal stream in 25 cases. In one-third of these cases it has been necessary to do another ileostomy, but if we have gained two-thirds of these it is, and has been, worth while.

For the benefit of the surgeon, ileostomies are best done as pull-through ileostomies. If a stab wound can be made through the entire abdominal wall and the ileum pulled up, that is the best type of ileostomy, for the following reason. Many of these patients will have lost 50, 60, or 70 pounds. If a longitudinal or transverse incision is made, then the ileum is pulled out in the incision and the colon removed, the patients will regain that weight. When, as so often happens, the incision is made in a patient who has had an appendectomy and has gained weight, there will be a deep valley with the scar at the bottom, filled up by fat on either side, about which it will be difficult to fit a Rutzen bag. Because of danger of prolapse, the mesentery of the ileum should be sutured to the parietal peritoneum in all deliberate ileostomies.

I would like to say again that we must do ileostomies earlier in patients who have ulcerative colitis with complications, that ileostomies permit patients to live completely normal lives, including being married and having babies, and that the high incidence of malignant disease in patients with long-standing ulcerative colitis and with their colons retained is something that should make us seriously think of removing all colons. The Koenig-Rutzen bag and other types of bags have converted these patients from a life of misery which was utterly impossible to one which, in this large number of patients on whom we have done ileostomies, is completely satisfactory and happy.

Lastly, the mortality of ulcerative colitis is not in the hands of any surgeon; it is in the hands of the family physicians and the gastroenterologists in terms of how soon they refer the patients for ileostomy when these serious complications are present.

"IT'S MY ALLERGY, DOCTOR"

At this time of the year, there are in many parts of the country an apparently unusual number of people with colds—colds which involve a great deal of sneezing, blowing, and tearing of the eyes. The phenomenon is quite easily explained however, as any follower of the little newspaper boxed notices headed "Pollen Count" can attest—it's merely the annual intensification of the hay fever season.

That the so-called allergic response typical of hay fever and allergic asthma may be due to any one of a large and varied number of activating agents is now understood. Much of the credit for the fundamental thesis of the mechanisms of the body response to allergenic agents has its basis in the work performed shortly before the end of the last century by a young French biologist—CHARLES RICHET.

Richet was conducting a series of experiments on the effects produced in laboratory animals by poisonous marine life. The story is now well known of how one of the dogs being used in the experiments reacted to a second injection of poisonous extract and subsequently died. Based on this and further experimentation, in 1902 Richet published a monograph in which he described his work and offered an hypothesis of the mechanism involved in what he termed "anaphylaxis." This hypothesis proved to be the foundation of the modern concepts of the causes and treatment of allergy.

Reprints of the Edmund Kopietz cover painting may be obtained on request to *Postgraduate Medicine,* 516 Essex Building, Minneapolis 3, Minnesota. Price $1.00.

The General Practice Review Section (page 125) is this month devoted to articles and a scientific exhibit relating to the management of allergic conditions.

Diagnostic Clinic

Diagnosis and Treatment of Segmental Neuralgia

WILLIAM BATES*

UNIVERSITY OF PENNSYLVANIA GRADUATE SCHOOL OF MEDICINE, PHILADELPHIA

We would like to present a couple of cases and inject them before going into any description, in order that you might see the actual working of such a case.

A little later on we will stress the examination of the back in every abdominal case before attempting to make a diagnosis, certainly examination before attempting any surgery for correction.

Dr. Judovich, will you demonstrate the areas of tenderness on this patient?

DR. BERNARD D. JUDOVICH: This patient is complaining of lower quadrant pain on the right side, associated with a zone of segmental tenderness. When segmental tenderness is found in association with pain it usually is derived from the region of the spine.

The area of pain takes in the lower quadrant, and associated with this is a tender area which also takes in the upper inner aspect of the thigh. If we squeeze this area she manifests pain. On the opposite side there is no such reaction. Here there is pain. If we go above this area, above the line, there is no tenderness whatsoever. Down inside the quadrant she is very sore; cross the midline and there is no tenderness.

Associated with this outline in front she has tenderness in the rest of the segment posteriorly. This takes in an area below on a level with the top of the trochanter, above from the costovertebral angle, coming down and overlapping the edge of the sacroiliac joint, and coming in across the line over the top of the trochanter. Below this line she exhibits no tenderness. Cross over the line and she is sore. The same is true up here; you can pinch her here, but come down below the line and she is sore. Pinch inside the margin of the sacroiliac joint and she is not tender. Lateral to it she is.

Finally, getting back to the actual source of the entire painful condition, she is tender at the right costovertebral angle and not on the left.

What we are going to attempt to do is a nerve block of the twelfth dorsal and first lumbar nerves which are causing this condition, and see if we can make the entire zone of tenderness and pain disappear following the nerve block.

DR. BATES: While the doctor is doing the nerve block, under this title of segmental neuralgia we want to call your attention to pain associated with tenderness. Pain without tenderness in the same distribution is not included within the scope of our cases.

This combination of pain and tenderness coexisting in definite segmental areas was originally discussed under the name of intercostal neuralgia. Later we called it parietal neuralgia, and more recently, segmental neuralgia was chosen as the best term.

My chief, the late Dr. J. B. Carnett, was the pioneer in this work of calling attention to associated pain and tenderness as indicative of parietal neuralgia rather than visceral pathology. In 1934 he had a paper prepared to read before this same group of physicians, but died before the paper was presented. I am back fifteen years later with what he might have had to say.

Just before the chief died in 1934, we found

*Professor of Surgery and Chairman, Department of Surgery, University of Pennsylvania Graduate School of Medicine, Philadelphia, Pennsylvania.

Presented November 2, 1949, before the meeting of the Interstate Postgraduate Medical Association of North America, Philadelphia, Pennsylvania.

an article by Frank of Germany, written in 1895, differentiating pain and tenderness in the abdominal wall from visceral pathology, which was very similar to Carnett's paper. More recently we have found an article written by a Frenchman for admission to the French Academy of Medicine in 1846, which was similar to the two later papers. I am certain that all three papers were the result of original thinking.

As a result of the line of thought developed by all three of these authors, it is imperative that when pain and tenderness are found in the abdominal wall one must differentiate them from possible tenderness of immediately underlying viscera. When tenderness is found in the course of routine abdominal examination, one thinks either of underlying viscera or of referred pain. By referred pain I do not mean pain due to contact with the peritoneum, but the type of referred pain that we think of in angina with its distribution in the chest wall and down the arm. That type of referred pain is practically never associated with segmental tenderness. It should cause us to think of something in the abdominal wall which may or may not be associated with visceral disease. In other words, the pain in the abdominal wall might be referred, but if there is associated tenderness, then we are dealing with something either in the abdominal wall or within the abdominal viscera.

That, of course, is a very different concept from the old Head-Mackenzie concept, but, as you know, both authors have retracted their original work and conclusions.

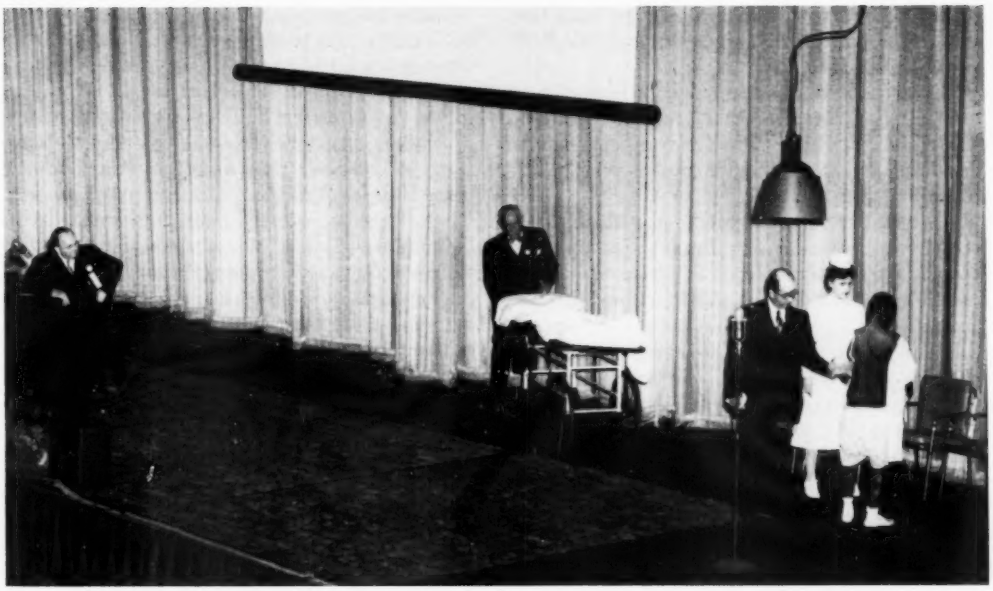
How do we differentiate pain and tenderness limited to the abdominal wall from visceral tenderness or from coexisting conditions where we have segmental neuralgia and visceral disease? Imagine a patient before you for abdominal examination. If with the abdominal wall relaxed you elicit tenderness, it may be either parietal or visceral. Now have the patient tighten the abdominal wall by blowing out, raising the head, or lifting the heels from the table. If tenderness is found with the abdominal wall tensed, at least some of the original tenderness found when the wall was relaxed is in the abdominal wall, because you cannot get your fingers through the tense muscles to feel the viscera. However, it does not mean that there is not also some visceral tenderness.

To complete the differentiation, then, it is necessary to block off sensation of the anterior abdominal wall. This can be done by paravertebral block with novocain, or, if you are concerned in the lower portion of the abdomen with the appendix or pelvic conditions—if pelvic, bilateral; if appendiceal, unilateral—inject novocain under the fascia of the external oblique. In a few minutes all sensation of pain and tenderness in the anterior abdominal wall is gone, the tenderness will disappear from the triangle high up on the inner side of the thigh, if there is no visceral disease underneath. But if there is disease underneath, such as an inflamed appendix, the tenderness resulting from pressure on the abdominal wall after injection of novocain will be much more marked than before, because the natural protectiveness of the abdominal wall is lessened by the injection. Therefore, you do not run the danger of complicating your picture by the blocking-out procedure.

After the injection of novocain, if a pinch of skin and superficial fat does not disturb the patient, then with the abdominal wall tensed, all tenderness of parietal origin should be gone.

If we now have the patient relax the abdominal wall and palpate again, we either find tenderness or no tenderness. If tenderness is present, then visceral disease must be suspected, but if all tenderness is gone, then all tenderness found before the novocain block was in the abdominal wall, because you cannot block off by local injection the tenderness of an inflamed structure. Again using the appendix for an example, with the rami communicantes from about the third dorsal to the second lumbar, and this being a unilateral organ with bilateral distribution of its nerve supply from the sympathetic, you would have to do injections all along the spine. This is the reason why in removing the appendix under local anesthesia, no matter how well the abdominal wall was anesthetized, you have to get some novocain into the mesoappendix.

I have constantly referred to the abdomen, but let me call your attention to the fact that all parts of the body are covered by a layer of parietes rich in sensory nerves which may confuse for deeper tenderness. Let me repeat, for the safety of future patients, parietal tenderness and visceral disease may coexist. Therefore, no matter how much you may believe in what we are trying to tell you, no matter how much you use it in your work—as we do every day and



Dr. Bates (at rostrum) discussing patient, assisted by Dr. Bernard D. Judovich (behind microphone). Dr. Mather Pfeiffenberger, Speaker of the Assembly, is shown at wheel cart.

have for years—you must constantly bear in mind that even though a patient has parietal tenderness, he may also have visceral disease. Otherwise, we will bring discredit to ourselves and to this type of diagnostic work.

DR. JUDOVICH: What we have done to the first patient is block the twelfth dorsal and the first lumbar nerve on the right. She has had it about three or four minutes, and these areas of tenderness seem to have disappeared. The left side now feels more tender than the right. In the area where she was quite tender, there is now no tenderness. The left side is now more apparent to her than the right, and this whole zone of segmental tenderness has subsided.

To get back to the cause of this condition, she has an increased lumbar lordosis, a scoliosis with the lumbar spine shifted to the left, because the left leg measures one-half inch shorter than the right, so that she has two types of strain here; she has lordosis and scoliosis, and she has torsion along with it.

The right hip is elevated as compared with the left, and the left buttock is slightly dropped. If she raises the heel the lumbar spine straightens out, but it does not correct the lordosis. This will have to be done with the aid of a support and exercises.

DR. BATES: If we were to go through this audience and take measurements we would find 4 people out of 7 with one leg shorter than the other. "Believe it or not" used to say that it is the reason a person walked in a circle in the woods, because one leg was shorter than the other. Be that as it may, we find clinically that a little over 50 per cent of people have one leg shorter than the other.

The causes of this parietal neuralgia which we are trying to call to your attention usually are present in two factors and require both of them to produce it, just as coagulation of blood in a vessel calls for a change in viscosity, a change in the rate of flow, or an injury to the intima—two of those factors are necessary to produce clot. Just so with parietal neuralgia; as a rule we have to have two factors. The commonest factors are infection above the clavicle, trauma, and postural defect.

A person may have a diseased gallbladder; he may have parietal neuralgia over the gall-

bladder, but removing the gallbladder does not remove the parietal neuralgia. It is an infection above the clavicle.

The second factor is trauma.

Third, the postural defect may be lordosis and scoliosis, which may be habitual, which may result from work, from careless posture, or it may be actually a short leg.

One may have any combination of these three factors, or a tumor or disease affecting the spine. Many of our metabolic disturbances have been found to be the cause for setting up this picture.

DR. JUDOVICH: This is a case of segmental neuralgia due to another cause. This patient complains of pain in the left leg. He has a scoliosis; he has some flattening of the spine; his body is shifted to the right; his reflexes are normal; however, he has hypesthesia of the left sciatic distribution and, what is important, tenderness at L-5, L-4 and L-5, and L-5 and L-1 spinous processes.

Bend forward with the knees straight. His forward bending is limited. He gets pain upon coughing, sneezing, and straining. Any act which increases intraspinal pressure produces pain. We feel that this is a case of ruptured intervertebral disk.

The treatment for these ruptured disks may vary greatly. In the past we operated on the greatest percentage of them, but our opinion has changed. We have been more conservative, because many of them will clear up with conservative therapy.

I am going to demonstrate the technic of a sciatic infiltration on this man.

DR. BATES: Remember in trying to make a differentiation of ruptured intervertebral disk that the irritation of the nerve tracts is central to the point of injection. Therefore, while the injection will do away with tenderness in the distribution of the trunks involved by the pressure from the disk, the pain that the patient has is not lessened because the injection does not travel that way in its effect. For differentiating these cases we are just as impressed as we are by x-ray as to whether or not a disk exists, because if we can get rid of the tenderness and not the pain and it is in the distribution of the usual disk, we feel pretty safe in our diagnosis. Repeated injections, however, while we are waiting for that disk to take care of itself—as it does in a great many cases—afford a great percentage of relief.

I heard a neurosurgeon say the other day that he thought that when we understood the cervical disk a little better it would simplify things, as the treatment of disk had simplified things in the lower extremities. In my language simplification is not spelled quite so easily, because I cannot conceive that a multiple diagnosis of cervical disk is going to lead to much happiness on the part of yourself or many patients. I believe, however, that when we understand the scalenus anticus syndrome as thoroughly as we do the disk syndrome of the lower extremity, we will be able to afford more relief, but I am not hoping for more cervical disk diagnoses.

In those cases where there is no visceral lesion for you to operate upon or to send to the surgeon, the segmental neuralgia must be treated to afford relief. In those cases where neuralgia and visceral disease coexist, after treating the visceral lesion the segmental neuralgia must be treated to prevent recurrence of symptoms which might lead to complication of visceral treatment.

I have seen 2 cases with 22 abdominal scars each. I had a case in the office yesterday with 13 abdominal scars. These 3 cases had their original symptoms when they came to us. An appendix is taken out because it is such a harmless thing to do, and then the tenderness persists afterwards and it is thought that possibly a sponge or an instrument was left, or a nerve was pinched, and the patient is sent back to the surgeon. He opens the abdomen, and if it happens to be a woman he does what any good surgeon does—he takes the tube and ovary out on that side. By the time the patient returns with the same pain, nothing is left on that side except the gallbladder, so he takes that out, and so it goes for innumerable operations, with failure to recognize that the symptoms were identical with those with which the patient first appeared.

I became very discouraged in my evangelistic work on this when a school teacher came to me after some operation and I raised her heel. She did not have to have injections; she got complete relief, but she disappeared, had another operation, came back, and I had to raise her heel because she had discarded it. She then had a baby and came back to get rid of her pain, and I had to raise her heel again. She then had a plastic operation, she again had pain, came back, and I had to raise the heel. When she

said, "Isn't it a curious thing that no matter what part of my body is operated on I have to come back to you to get relief?" I sort of threw up my hands.

If this combination exists we feel that the segmental neuralgia is often the cause of the repeated unsuccessful and unnecessary operations. The cure or prevention of recurrence is to find and eliminate the cause. In other words, I don't think we have as many operative failures as we have errors in preoperative diagnosis. I think we try to fit patients to our abilities to treat instead of getting down to grass roots and really finding out what the situation is. If it is infection, it must be brought under control. If it is trauma, it must be handled and if possible prevented in the future. If it is postural, it is usually associated with a marked lordosis or scoliosis of the spine. If it is lordosis, Goldthwaite's exercises are indicated. Roughly, the Goldthwaite exercises are 1, 2, 3—front porch back, dining room upstairs, sitting room down, in order to straighten the spine.

In scoliosis, if not fixed by previous disease the probability is that it is due to one leg's being shorter than the other. These cases we correct by raising the heel on the short side. Please do not undercorrect and please get away from the old, old idea that overcorrection is going to help. Once you correct the heel you ought to see that patient not less than every six months because the change in the length of the extremity is usually the angle at the hip, and once you raise the heel, the other hip may seek the same angle and you will have pain on the same side or, more often, on the opposite side. The raised heel should be looked at at least every six months. Measurements can be made by x-ray with the patient standing and having a line across your field with a water level on it, using a steel tape measure, or by placing blocks of known thickness under the heel until the spine is straight.

If pain and tenderness persist after correcting known lesions, we then do paravertebral injections of the segments involved. These injections are some variety of sulfate solutions which we have worked out in the laboratory, usually 0.75 per cent ammonium sulfate in a buffer vehicle.

If after three injections no lasting effect is afforded, the whole cause has probably not been relieved and the patient must be restudied.

For the purposes of this discussion, the important thing is to recognize the presence of segmental neuralgia to prevent unnecessary studies, needless operations, and to afford patients relief of pain.

Are you ready to demonstrate the difference in tenderness in this patient, Dr. Judovich?

DR. JUDOVICH: I have done a left sciatic injection on this man. The technic is to measure from the top of the trochanter to the posterior superior spine, get the midpoint, come down about an inch and a quarter and go directly down to the sciatic notch. Formerly we did paravertebral blocks, but clinically this serves just as well.

It is hard for him to stand up just now—that left leg won't support him—it is knocked out for the time being and has lost its tenderness—but it does cause complete relaxation and very often you get an analgesia extending up into the root itself with quiescence of tenderness over the spinous process.

DR. BATES: What did you inject with?

DR. JUDOVICH: We injected a mixture of 2 per cent procaine and ammonium sulfate.

DR. BATES: That leg is knocked out now because of the procaine and not because of the ammonium sulfate.

DR. JUDOVICH: Right.

DR. BATES: The injection of ammonium sulfate, whether it is used intraspinally, paravertebrally, or in the nerve itself, has no effect on motor nerves. It is absolutely selective for the C or pain fibers of peripheral nerves. The C fibers are the unmyelinated fibers which carry pain alone. The injection does not interfere with vibration, heat, cold, touch, or any of the sensations. It simply interferes with pain conveyance, and in those cases where we use it we have no fear of motor involvement. That has all been worked out in the cathode chamber on the femoral nerve of the cat, and if something happens to the motor nerves it is certainly not due to the ammonium sulfate solution.

Case Report

The Liver-Kidney Factor in Unexpected Surgical Deaths

H. THURSTON WHITAKER[1] AND WILLARD H. PARSONS[2]

THE LUTHERAN HOSPITAL AND VICKSBURG CLINIC, VICKSBURG, MISSISSIPPI

Boyce was, of course, expressing his own convictions, but he was also summing up the opinion of a number of other observers when in 1941 he wrote the following sentences:[1]

> In failure to comprehend the risks of unsuspected hepatic dysfunction in superficially good risk patients, in failure to correct hepatic dysfunction in patients with frankly damaged livers, undoubtedly lies the explanation of a certain unexpected postoperative morbidity and a certain unexpected surgical mortality. The depression of hepatic function which occurs after any sort of surgery is both the explanation of such catastrophes and the clue to the means by which they can be avoided.

We greatly fear that the following case history illustrates only too well the "unsuspected surgical mortality" which may originate from unsuspected liver damage in a patient who presents a superficially good surgical risk.

CASE REPORT

A 45-year-old white man was admitted to the Vicksburg Hospital July 5, 1947, with a nine-month history of dyspepsia characterized by epigastric pain, flatulence, nausea, vomiting, and moderate loss of weight. For the past year he had had nocturia (three times nightly) and some burning on urination. Otherwise his previous history was not relevant.

The general physical examination was essentially negative. The patient was well nourished and presented no evidence of loss of weight. Abdominal examination elicited no pain, tenderness, rigidity, or masses. The prostate gland was normal in all respects. The blood pressure was 138/70. The temperature, pulse, and respiration were within normal ranges.

Urinalysis revealed 2 plus albumin on the first examination but no albumin on subsequent (daily) examinations. The specific gravity was 1.020. The first microscopic examination of the urine showed 5 to 10 white blood cells and occasional red blood cells per high-powered field but on subsequent examinations both varieties of cells appeared only occasionally. A complete blood count, a determination of the serum protein level and albumin-globulin ratio, and gastric analysis revealed no abnormalities. The nonprotein nitrogen of the blood was 41.3 mg. per cent and the creatinine was 1.5 mg. per cent.

Roentgenologic examination of the gastrointestinal tract with a barium meal revealed a nonobstructing carcinoma on the greater curvature of the stomach, at the junction of the proximal and middle thirds. A calcified tubercule was thought to be present in the right upper lung field but otherwise roentgenograms of the chest revealed nothing abnormal.

The patient was regarded as a good surgical risk and therefore received only routine preparation for a gastrointestinal operation, though arrangements were made for ample quantities of blood to be available during and after surgery.

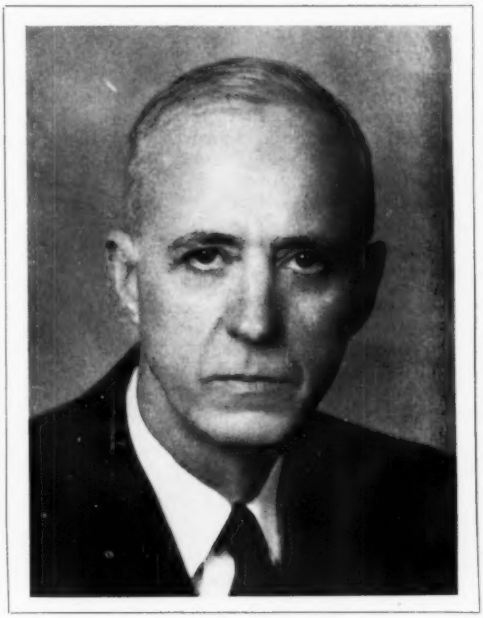
On July 14, under ether-oxygen anesthesia, with pentothal sodium induction, a radical subtotal gastrectomy was performed for a malignant growth in the location visualized in the roentgenograms. Careful exploration revealed metastasis to a single omental lymph node which was excised together with the omentum. No nodules could be felt in the liver, which was entirely normal in size, color, and consistency. Whole blood in the amount of 1,000 cc. was given by continuous transfusion during the course of the procedure, though very little blood was lost. The blood pressure scarcely deviated from the preoperative level until just before the conclusion of the operation, when it fell to 95/88. The pulse, which had previously been 90 to 100 and of good volume, now became rapid and irregular.

The patient was slightly cyanotic when he was returned to his bed, but the Trendelenburg position and the administration of oxygen by nasal tube produced almost immediate good results. The color returned to normal, the pulse became strong and regular, and the

[1]Fellow in Surgery, The Lutheran Hospital and The Vicksburg Clinic, Vicksburg, Mississippi.

[2]Chief of Staff and Director of Surgery, The Lutheran Hospital and The Vicksburg Clinic, Vicksburg, Mississippi.

H. THURSTON WHITAKER



WILLARD H. PARSONS

blood pressure returned to approximately the preoperative level (136/70). The postoperative regimen included penicillin, amigen (500 cc.) and dextrose-physiologic salt solution (1,000 cc.) by infusion.

The temperature rose to 102.4° F. the night of operation. The patient voided 200 cc. of pale yellow urine voluntarily. His general condition seemed good and he had a comfortable night.

About thirty hours after operation the patient suddenly became restless, dyspneic, and cyanotic and went into a state which would have been termed shock except that the oral temperature, in spite of measures to control it, rose steadily to 104.6° F. The blood pressure was 82/70 and the pulse 136. Atelectasis was considered to be the most probable diagnosis, although clinical examination of the chest furnished no support for it and roentgenograms with the portable machine showed both lung fields normal.

Treatment consisted of the administration of 500 cc. of whole blood, 1,000 cc. of plasma, and 2,000 cc. of glucose in physiologic salt solution. Oxygen was given continuously. After several hours the signs and symptoms suggestive of shock almost disappeared. The temperature remained at 104.6° F. (by mouth) in spite of measures to reduce it. The twenty-four-hour urinary output was 650 cc.

The patient spent another fairly good night, except for the persistent elevation of temperature, but in the morning (forty-eight hours after operation) the shock-like state again supervened. The blood pressure again fell, and the pulse, which was barely perceptible, was thought to be about 140. The respiration was 40 per minute and very shallow. The patient was cyanotic and extremely dyspneic. Treatment consisted of the administration of 2,000 cc. of whole blood and 500 cc. of 25 per cent glucose with aminophylline. Oxygen had been given continuously since the shock-like episode eighteen hours earlier. Only 25 cc. of urine was obtained by catheterization, making a total urinary output of 875 cc. in the forty-eight-hour period since operation. The patient's condition deteriorated steadily and death occurred fifty-two and one-half hours after he had been removed from the operating table.

Autopsy—Postmortem examination, which was carried out immediately, revealed the chest clear, except for the nodules to be described later, and the operative site in good condition, with no evidence of leakage at the anastomosis or elsewhere. The peritoneal cavity was perfectly clean.

The liver, in startling contrast to its completely normal appearance at operation, was now enlarged, with slightly rounded edges. Its surface was greasy, as was its substance on section. Careful examination revealed no gross evidence of metastases. Histologic examination confirmed the absence of metastases. The liver cells were swollen and irregular in outline. Their cytoplasm was granular in appearance and showed droplets of fatty metamorphosis. Their nuclei showed chromatolysis and karyorrhexis.

THE gross description of the kidneys was as follows: The right kidney weighs 325 gm. and the left 150 gm. Arising from the upper part of the right kidney is an oval, well-encapsulated mass measuring 14 by 10 by 8 cm. On surface bisection this mass is

seen to involve most of the kidney substance and to consist of grayish-red to yellow tissue which is moderately firm in some areas and in others is friable and contains scattered cystic spaces and small hemorrhages. The tumor mass does not involve the pelvis of the kidney on this side and the recognizable portion of the kidney substance is grossly normal. The capsule of the left kidney strips with ease, leaving a smooth, grayish-pink surface. The only abnormality seen on this side is a sharply circumscribed nodule, about 3 cm. in diameter, situated near the lower pole on the anterior surface. It is made up of moderately firm, grayish-red tissue.

Histologic examination revealed the tumor in the right kidney to be a hypernephroma and the nodule in the left kidney to be a metastasis from it. Two similar circumscribed metastatic nodules were found in the apex of the right lung. Histologic examination of sections of the kidneys also showed marked degenerative and nephrotic changes in the convoluted tubules of both organs. The individual cells were swollen and irregular in outline and projected into the lumina of the tubules. Some were completely disintegrated. Their cytoplasm was faint but highly granular in appearance. Their nuclei showed chromatolysis and karyorrhexis. There was considerable hyperemia of the intertubular capillaries.

Pathologic examination of the excised specimen from the stomach revealed an ulcerative adenocarcinoma involving the greater curvature and anterior wall at the junction of the proximal and upper thirds. Histologic study revealed it to be grade III by Broders' classification. The excised omental lymph node contained metastatic tissue from the gastric tumor.

POSSIBLE FACTORS OF MORTALITY

A totally unexpected fatality such as occurred in this case is always a bitter blow to the surgeon. If he is conscientious, he cannot avoid a careful stock-taking, to see wherein he erred and how the tragedy might have been prevented. In retrospect, however, this case presents many puzzling aspects.

Before operation the patient was regarded as a good surgical risk, so good, in fact, that he was given only routine (though fully adequate) preoperative preparation for the gastrectomy contemplated. Although he had a nine-month history of symptoms clearly referable to gastric carcinoma, he had no visible signs of the disease and his nutritional status was excellent. Because albuminuria was present only transiently, no detailed study of renal function was made. Herein we erred. The slightly elevated nonprotein nitrogen of the blood offered a warning which we did not heed.

The patient obviously did not die from carcinoma of the stomach, the only metastasis from which, as confirmed by autopsy, was to a single omental lymph node. The hypernephroma found at autopsy was a completely unexpected finding. It occupied a large portion of the substance of one kidney, but the metastasis to the other was well circumscribed and it does not seem reasonable to ascribe to this tumor the oliguria which was a prominent feature of the postoperative course. The circumscribed pulmonary metastases from the renal neoplasm also can be discounted.

The operation was long and somewhat difficult, it is true, but apparently adequate oxygenation was maintained throughout and the amount of blood administered during the procedure was considerably more than the amount apparently lost. Typing and cross-matching had been carefully carried out and neither then nor later did anything remotely suggestive of a transfusion reaction occur. Death was precipitated by the surgery performed but was not caused by it in the sense that technical errors or infection could be blamed.

The moderate degree of shock which occurred fifteen minutes before the operation was concluded was promptly corrected by standard measures and within an hour the patient's condition seemed perfectly satisfactory. The two subsequent shock-like episodes, the last of which was fatal, developed suddenly. They were typical of shock in most respects except that the persistent hyperpyrexia which was associated with them is no part of the picture of true shock. Within eight hours after operation the temperature was 102.8° F.; within thirty hours it was 104.6° F., and it remained at that level, in spite of energetic measures to reduce it, until death.

Clinically the striking features of the postoperative period were the hyperpyrexia just described and the progressive oliguria. The most striking feature of the autopsy, in addition to the entirely unexpected finding of a second malignant tumor in the right kidney, was the remarkable deterioration which had occurred in the liver within the fifty-two and one-half-hour period between operation and death. Within this brief time a grossly normal and healthy organ had enlarged perceptibly and had undergone gross fatty metamorphosis. Histologic examination was not needed to establish the change; mere inspection revealed the unhealthy, greasy appearance. Postmortem changes do not explain the alteration. For one thing, autopsy was performed promptly after death, and for another, fatty metamorphosis is not a typical postmortem change. The kidneys, in addition to being the site of malignant changes in certain areas, presented degenerative and nephrotic changes in the convoluted tubules.

THE HEPATORENAL SYNDROME

The course of events during this patient's brief period of survival after operation and the alterations found in the liver and the kidneys at operation in our opinion establish the cause of death in this case as the so-called liver-kidney or hepatorenal syndrome, first described by Heyd[2] in 1924 and

later amplified, experimentally and clinically, by Connell,[3] Petren,[4] Helwig and Schutz,[5] Boyce,[1] and Schmidt and Chesky,[6] among others. The hypernephroma found at autopsy introduces an extraneous note, but otherwise the only difference between this case and the many cases of liver or liver-kidney death described by these observers is that in this case the renal factor became evident almost simultaneously with the hyperpyrexia, whereas usually it appears later.

Schmidt and Chesky[6] are almost the only writers on the subject of the hepatorenal syndrome who believe that in this postoperative complication the secretory activity of the kidney is compromised earlier, and to a greater degree, than hepatic function is compromised after operation. Nine of the 10 patients in their series had evidence of decreased liver function within twenty-four to forty-eight hours, but in half of these cases oliguria developed in twelve hours, in spite of an adequate fluid intake. In this respect their cases are similar to ours. These same observers mention that 5 of 7 patients who developed postoperative hypotension had had transient falls to shock levels while they were on the operating table. Again the course of events which they describe is the same as in our case, though their criterion of the hypotension of shock (70 millimeters of mercury systolic or less) is considerably below the level experienced by our patient during the episode of shock on the operating table as well as during the first episode after operation.

ROLE OF LIVER DAMAGE IN SURGICAL MORTALITY

There is no longer any doubt that liver damage, which is expressed clinically in certain syndromes and expressed in the laboratory in terms of decreased hepatic function as revealed by various tests, is an extremely important consideration in the surgical patient. Heyd's[2] first observations on this subject were based on an eighteen-month study in which the liver was examined every time the abdomen was opened and in which biopsy specimens were secured in many cases. He had a sound background, therefore, for his conclusion that hepatitis is almost invariably associated with disease of the gallbladder and bile ducts.

These pioneer observations have since been amply confirmed. Lahey,[7] for instance, has stated that the mortality of gallbladder disease is largely in the liver, just as the mortality of prostatic disease is largely in the kidney. Ravdin and his associates,[8] by studies on the bile acids, found hepatic damage in all patients in whom complete biliary tract obstruction had been present for a week or more. Graham[9] made an extremely practical contribution to the problem when he observed that an unusual degree of dye retention in tests carried out before operation was the only common factor in 4 entirely unexpected deaths following biliary tract surgery. Thereafter he refused to operate upon patients with a high degree of retention until the amount of dye retained had been reduced to normal levels.

THERE are probably few present-day surgeons who are not very well aware that hepatic damage is likely to exist in biliary tract disease and who do not take steps before operation to protect their patients against its possible consequences. There is far less realization of the fact that, as happened in our own case, liver damage may also exist in diseases not related to the biliary tract. Yet numerous studies show that it is frequently present in other conditions and that not infrequently, as in our own case, it seems to play the major role, or the sole role, in the fatality.

Numerous observers have pointed out the role played by the liver in toxic thyroid disease, and so experienced a thyroid surgeon as Lahey[10] has said that as his experience has increased, he has become more and more sure that deaths caused by hyperthyroidism are chiefly liver deaths.

Boyce[1] has brought together from the literature numerous convincing illustrations, and has added other cases, of the role of the liver in nonbiliary tract disease, including burns, intestinal obstruction, and various types of malignant disease. He has also collected numerous instances of liver or liver-kidney deaths following operations of various kinds, including even appendectomy for chronic appendicitis.

The anesthetic factor—One consideration which cannot be ignored in the case under discussion is the anesthetic factor. The anesthetic agent was ether and the duration of the procedure three hours. It was thought at the time of operation that oxygenation was adequate, but what happened afterward suggests that perhaps we were mistaken. The oxygen given in high concentrations almost continuously after operation perhaps was not sufficient to counteract the effects of inadequate oxygenation at operation. Certain clinical and experimental studies[1] are of interest in this connection.

Without exception these studies show that all volatile anesthetics affect the liver to some degree, the adverse effect being more marked in experimental animals if they have been fasted before they are anesthetized. They also show that the effect of the anesthetic is more pronounced in livers which are the site of disease, or which are glycogen-poor or fat-rich or both. Finally, these studies show that the degree of damage depends upon the intensity of the narcosis rather than the duration, and depends even more upon the degree of oxygenation maintained during anesthesia. The studies of Goldschmidt, Ravdin and their associates,[11-13]

which were carried out with competent anesthesia on dogs in good condition, are particularly convincing on all of these points and their data seem to throw some light on what may have happened in our own case.

Hemorrhagic shock—Among recent studies of liver damage, one by Fine and his associates[14] concerning the effect of hemorrhagic shock might also be mentioned. These observers were able to show that the removal of an amount of plasma which would ordinarily be well tolerated results in rapidly fatal shock if it is repeated after the liver is slightly damaged. Experiments on perfusion of the liver via the splenic vein with arterial blood during shock led them to conclude, further, that the liver is the organ directly responsible for failure of the peripheral circulatory apparatus in shock. It is doubtful that this hypothesis can be applied in toto to our case, for a number of reasons. The clinical picture, as already noted, while it was shock-like, was associated with hyperpyrexia not at all typical of shock. The blood lost at operation was more than replaced and was, indeed, replaced as it was being lost, while additional quantities of blood were given after operation, when there was no evidence at all of hemorrhage, an assumption confirmed by the postmortem findings.

Pigment nephropathy and lower nephron nephrosis—It is impossible to disregard, in a discussion of this case, the pigment nephropathy reported in battle casualties during World War II, which was clearly related to the so-called crush syndrome first reported from England following enemy air raids. Snyder and Culbertson[15] recently discussed in detail the 99 deaths from this cause which had occurred in 1,411 deaths in Fifth Army hospitals in Italy. In 68 of the 99 deaths no cause for the fatality other than renal changes could be found. In the remaining 31 cases, as well as in 57 other cases not included in the series, pigment nephropathy was not the sole cause of death but had clearly contributed to the fatal outcome.

It seems highly unlikely, however, that the pigment nephropathy observed in these cases could explain the fatality in our case. The circumstances were, in fact, widely different. All the soldiers in the Snyder-Culbertson series had been in severe shock but all were apparently well along on the road to recovery from it and from their wounds when progressive oliguria and anuria developed. Death usually occurred between the fourth and eighth days after wounding. Gross infection was evident in 61 of the 99 cases. Frank renal trauma was present in 18, and the ureter had been traumatized by the original injury or had been accidentally tied at operation in 3 others.

The authors concluded that shock was the only common factor in their 99 cases. They also state, on the basis of a comparison of microscopic sections, that the hepatorenal syndrome described by Helwig and Schutz[5] is the same condition as the pigment nephropathy which they describe. The liver factor, however, was not present in all of Snyder and Culbertson's cases and they do not emphasize it. It may be significant, on the other hand, that toxic hepatic degeneration was noted in 16 cases in their series, epidemic hepatitis in 4 cases, and septic hepatic degeneration secondary to trauma in 2 cases. Epidemic hepatitis was possibly present in 1 additional case and septic hepatic degeneration was possibly present in 3 other cases.

The clearcut alteration in the liver present in our own case does not seem to have occurred in any of Snyder and Culbertson's cases. The profound shock initially present in most of their cases is not comparable to the moderate, transient shock present at the close of the operation in our own case. Moreover, the gross infection evident in 61 of the 99 cases in the Snyder-Culbertson series makes a comparison of their series with other instances of the hepatorenal syndrome, such as our own case, not altogether valid. Infection played no part whatsoever in our case, and Boyce[1] and others have emphasized that cases in which infection is a factor cannot be considered true examples of liver death or the liver-kidney syndrome.

The instances of combat-derived pigment nephropathy just discussed naturally bring to mind the similar so-called lower nephron nephrosis which has attracted so much attention in the recent medical literature. The contribution of Coller and his associates[16] may be cited as typical. These authors, like others who have written on the subject, do not adduce a possible liver factor to explain the condition. They do not mention the liver, in fact, in the protocols of the specimen cases in which fatalities occurred and in which they attribute the underlying cause of death to such factors as shock, hemolysis following blood transfusion, and various injuries.

As we have already noted, blood transfusion can be eliminated as a factor in our case, the initial shock was moderate and was overcome well within the limits (two to three hours) set by various observers as the safe period for established shock, while the startling change which occurred in the liver between operation and the postmortem performed immediately after death simply cannot be disregarded in the explanation of the fatality.

The concept of the "liver weakling"—The underlying explanation of the death which occurred in this case can perhaps be found in what has been termed the concept of the "liver weakling." First advanced by Henschen,[17] Rozendaal, Comfort and Snell,[18] Hurst, Weir,[19] and others, it has been accepted by numerous observers, who advance the

point of view that liver damage is by no means infrequent in the general population and, to quote Boyce,[1] is at least a possibility in any surgical patient, regardless of his immediate pathologic process. The corollary to that belief is that the individual with a damaged liver is a dubious candidate for any sort of surgery. In spite of the lack of gross evidence of pre-existent liver damage, it does not seem unreasonable to assume that herein lies the fundamental explanation of our patient's death.

THE PREVENTION OF LIVER (LIVER-KIDNEY) DEATHS

If the concept of the "liver weakling" is accepted, its implications must also be accepted. The status of the liver must be determined before any operation is performed, or routine preoperative protection of the liver must be instituted, or, preferably, both of these plans must be adopted. It is no longer possible to dismiss the whole matter with the statement that tests of liver function are not reliable, or that the liver has so many different functions that no single test reveals them all.

It is true that very few tests of liver function are as reliable as they might be. It is also true that many of them have not been given adequately controlled trials. Moreover, the selection of the tests appropriate for any single case often introduces difficulties which are not in any way resolved by the performance of numerous promiscuous tests on the same patient. These considerations are important even in large hospitals, in which laboratory facilities and personnel, though sometimes hard-pressed, are usually ample for whatever may be required. The death we are discussing, however, occurred in a small hospital, in which laboratory facilities and personnel, though ample, must be conserved and used with discretion.

Our own opinion is that under these circumstances, the practical necessities of the situation can best be met, and the patient's interests can best be served, by the comparative performance of two tests, the intravenous dye excretion test by the Macdonald technic and the Quick hippuric acid test, preferably by the intravenous route.[20-21] If these two tests reveal apparently normal liver function, it seems reasonably safe to conclude that the patient, from this standpoint, is a fit surgical risk. If either test, or both, should reveal depression of liver function, appropriate corrective measures should be instituted and the tests should be repeated serially until liver function has been restored to an apparently safe level. Opinions may differ as to the comparative value of these and other liver function tests, but those who have had a wide experience with them report them simple and efficient and testify that as experience with them increases, and their interpretation becomes more accurate, they become more useful.

The next question is what to do for the patient who displays a moderate or minimal preoperative depression of liver function, or for the patient in whom no liver function tests at all have been performed. An elaborate preoperative regimen of intravenous therapy would certainly not be justified in patients in these groups. It would impose an intolerable burden on hospital personnel. It would be very expensive for the patient (or for the hospital, if the patient were indigent). Finally, it would not be free from risk. No matter how much care is exercised, reactions, sometimes catastrophic, may follow transfusions and other forms of intravenous therapy and their employment on slight or nebulous indications is not warranted.

Such elaborate measures, however, are not necessary. Althausen,[22] among others, has emphasized that the simplest way to introduce food elements into the body is by the natural route, that is, by mouth. Boyce[1] has shown that when patients are fed dextrose by mouth before operation, the depression in liver function which occurs after anesthesia and operation is likely to be less marked and less prolonged than when dextrose is given by vein. This same observer describes an extremely toxic hyperthyroid patient whose liver function (by the Quick oral test) was increased more than 23 per cent over a two-week period before operation by the simple addition of sugar to her breakfast cereal and jelly to her luncheon diet.

All the evidence seems to suggest that a considerable measure of protection can be furnished the patient in whom intravenous therapy is not warranted by increasing the amount of protein in the daily diet, adding dextrose to it in the form of soft drinks, sweetened fruit juices, jelly and hard candy, and maintaining an adequate state of hydration.

We do not believe that we are unduly complacent when we say that it seems to us that our postoperative therapy in the case we are reporting was fundamentally correct in principle and reasonably energetic in application. The patient received 2,500 cc. of fluid (including blood) the day of operation, 3,500 cc. (including plasma) the following day, and 2,500 cc. (including 2,000 cc. of blood) the day of death. Writers[17,23,24] on the subject of lower nephron nephrosis may differ in the exact methods of treatment which they advise, but all are agreed that the objective should be to keep the patient alive until the damaged tubules of the kidney recover spontaneously. Undoubtedly this is sound advice, but we do not believe that in this case the condition was a pure lower nephron nephrosis. We agree with Strauss[23] that it is highly unlikely that renal insufficiency per se could lead to death within six days, and it seems, therefore, even more improbable that it could produce it

within fifty-two and one-half hours, the period which our patient survived after operation.

One postoperative measure which we did not employ and which, in retrospect, we think that we should have employed, is decholin sodium. Schmidt and Chesky[6] had favorable results with it in several of their cases and Boyce reported striking results with it in an occasional instance of the hepatorenal syndrome observed after operation, as well as in cases of depressed liver function identified before operation.

SUMMARY AND CONCLUSIONS

A case has been described in which gastrectomy for resectable carcinoma of the stomach, under ether anesthesia, was followed by hyperpyrexia, oliguria, and death within fifty-two and one-half hours, apparently, as confirmed by postmortem examination, from the hepatorenal syndrome. The fundamental error in this case was clearly the assumption that a patient who *appeared* to present a good surgical risk *actually* presented it. No preoperative study was made of the liver function. No preoperative routine was instituted which would have protected the liver against the trauma of surgery and the toxic effects of prolonged ether anesthesia. The functional reserve of the kidneys was not investigated, although the slight increase in the nonprotein nitrogen of the blood furnished a warning in this regard which was not heeded.

These were natural errors of omission; they are made hundreds and even thousands of times without serious consequences. But in this particular case the insults of operation, of anesthesia, and of a limited period of anoxia were more than the functionally depressed liver and kidneys could tolerate. The startling difference between the grossly normal liver examined at operation and the grossly abnormal organ found at postmortem examination slightly more than fifty hours later seemed to leave no doubt of the source of the fatality.

An analysis of the factors of mortality in this case suggests the necessity, even in apparently good risk cases, of preoperative study of the liver function and of preoperative, as well as postoperative, protection of the liver against the strain imposed by surgery and anesthesia. If the concept of the "liver weakling" be accepted, the institution of simple preoperative preparation seems wise in any patient to be submitted to a major surgical procedure, regardless of how good his status may seem.

REFERENCES

1. Boyce, Frederick F.: The Role of the Liver in Surgery. Springfield, Illinois, Charles C Thomas, 1941.
2. Heyd, C. G.: The liver and its relation to chronic abdominal infection. Ann. Surg. 79:55-77 (January) 1924.
3. Connell, C. G.: Liver death (so-called). Rapid high temperature deaths. Ann. Surg. 100:319-327 (August) 1934.
4. Petren, G.: On the causes of post-operative deaths. Ann. Surg. 92:1-7 (July) 1930.
5. Helwig, F. C., and Schutz, C. B.: A further contribution to the liver-kidney syndrome. J. Lab. & Clin. Med. 21:264-277 (December) 1935.
6. Schmidt, C. Robert, and Chesky, V. E.: Clinical studies of liver function. The hepatorenal syndrome. Am. J. Surg. 75:772-795 (June) 1948.
7. Lahey, F. H.: The present management of biliary tract disease. S. Clin. North America 12:549-564 (June) 1932.
8. Ravdin, I. S., Johnston, C. G., Riegel, C., and Wright, S. L.: A study of human liver bile after release of common duct obstruction. J. Clin. Investigation 12:659-672 (July) 1933.
9. Graham, E. A.: Lowering the mortality after operations on the biliary tract. Illinois M. J. 60:196-202 (September) 1931.
10. Lahey, F. H.: The reduction of the mortality in hyperthyroidism. New England J. Med. 213:475-479 (September 5) 1935.
11. Goldschmidt, S., Vars, H. M., and Ravdin, I. S.: The influence of foodstuffs upon the susceptibility of the liver to injury by chloroform, and the probable mechanism of their action. J. Clin. Investigation 18:277-289 (May) 1939.
12. Ravdin, I. S., Vars, H. M., Goldschmidt, S., and Klingensmith, L. E.: Anesthesia and liver damage. II. The effect of anesthesia on the blood sugar, the liver glycogen, and liver fat. J. Pharmacol. & Exper. Therap. 64:111-129 (September) 1938.
13. Goldschmidt, S., Ravdin, I. S., and Lucke, B.: Anesthesia and liver damage. I. The protective action of oxygen against the necrotizing effect of certain anesthetics on the liver. J. Pharmacol. & Exper. Therap. 59:1-14 (January) 1937.
14. Fine, Jacob, Seligman, Arnold M., and Frank, Howard A.: On the specific role of the liver in hemorrhagic shock. Report of progress to date. Ann. Surg. 126:1002-1009 (December) 1947.
15. Synder, Howard E., and Culbertson, James W.: Pigment nephropathy in battle casualties. Arch Surg. 56:651-671 (May) 1948.
16. Coller, Frederick A., Campbell, Kenneth N., and Iob, Vivian: The treatment of renal insufficiency in the surgical patient. Ann. Surg. 128:379-390 (September) 1948.
17. Henschen, C.: Cited by Boyce.[1]
18. Rozendaal, H. M., Comfort, M. W., and Snell, A. M.: Slight and latent jaundice. The significance of elevated concentrations of bilirubin giving an indirect van den Bergh reaction. J.A.M.A. 104:374-379 (February 2) 1935.
19. Weir, J. F.: Hepatitis. Some forms not commonly recognized. J.A.M.A. 111:1356-1362 (October 8) 1938.
20. Macdonald, D.: A practical and clinical test for liver reserve. Surg., Gynec. & Obst. 69:70-82 (July) 1939.
21. Quick, A. J.: Intravenous modification of the hippuric acid test for liver function. Am. J. Digest. Dis. 6:716-717 (December) 1939.
22. Althausen, T. L.: Dextrose therapy in diseases of the liver. J.A.M.A. 100:1163-1167 (April 15) 1933.
23. Strauss, Maurice B.: Acute renal insufficiency due to lower-nephron nephrosis. New England J. Med. 239: 693-699 (November 4) 1948.
24. Hoffman, William S., and Marshall, Daniel: Management of lower nephron nephrosis. Report of six cases. Arch. Int. Med. 83:249-270 (March) 1949.

Scientific Exhibit

Cortisone*

J. M. CARLISLE, M. D., A. GIBSON, M. D., AND E. SCHMATOLLA, M. D.

MEDICAL DIVISION, MERCK & CO., INC., RAHWAY, NEW JERSEY

Cortisone* is one of the series of crystalline hormonal substances isolated from extracts of the adrenal cortex in the laboratory of Dr. E. C. Kendall of the Mayo Foundation. This substance, originally named compound E, was isolated from beef adrenal glands and described by Mason, Myers and Kendall in 1936. It was also described independently by Reichstein as substance FA, and by Wintersteiner and Pfiffner as compound F.

Cortisone was first synthesized from a bile acid in 1946 by Dr. L. H. Sarett of the Research Laboratories of Merck & Co., Inc. The availability of cortisone in sufficient quantities for clinical use was the result of a practical synthesis developed by the combined efforts of Dr. Kendall and his associates and of Dr. Max Tishler and his associates in the Merck Research Laboratories.

*Cortisone is supplied by Merck and Co., Inc., under the trade-mark name CORTONE.

Scientific Exhibit awarded Certificate of Merit in the Scientific section at the American Medical Association convention, San Francisco, June 26-30, 1950.

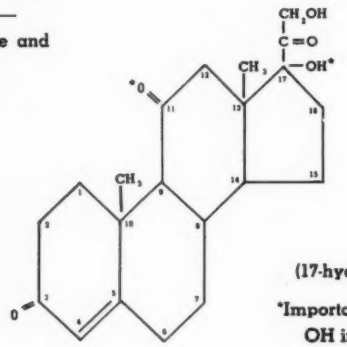
CHEMISTRY OF CORTISONE

STRUCTURAL RELATIONSHIP TO OTHER ADRENAL CORTICAL STEROID HORMONES

CORTISONE, a physiologically active adrenal cortical steroid. Originally named Compound E. The principal member of the 11, 17-oxysteroid group, one of the three main groups of physiologically active adrenal cortical steroid hormones.

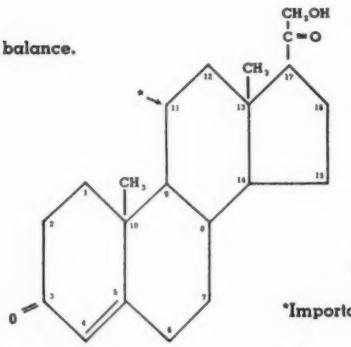
PRINCIPAL GROUPS OF ADRENAL CORTICAL HORMONES

11- and 11,17-oxysteroid group —
affect chiefly carbohydrate and protein metabolism.



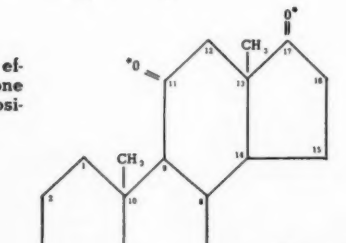
CORTISONE
(17-hydroxy-11-dehydrocorticosterone)
*Important features – 0 atom in position 11, OH in position 17

11-desoxy group —
affect chiefly electrolyte balance.



Desoxycorticosterone
(11-desoxycorticosterone)
*Important feature – no 0 atom in position 11.

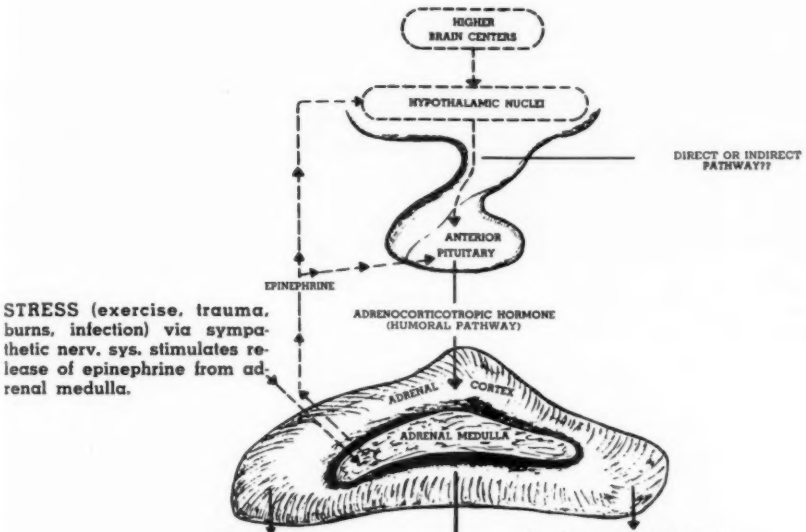
Adrenal androgens —
androgenic and anabolic effect; related to testosterone but have an 0 atom in position 11.



Adrenosterone
*Important features – 0 atom in position 11, 0 atom in position 17 hence 17-ketosteroid.

PITUITARY ADRENAL RELATIONSHIPS

THE SECRETION OF CORTISONE* AND RELATED ADRENAL STEROIDS


HIGHER BRAIN CENTERS
HYPOTHALAMIC NUCLEI
DIRECT OR INDIRECT PATHWAY??
ANTERIOR PITUITARY
EPINEPHRINE
ADRENOCORTICOTROPIC HORMONE (HUMORAL PATHWAY)
STRESS (exercise, trauma, burns, infection) via sympathetic nerv. sys. stimulates release of epinephrine from adrenal medulla.
ADRENAL CORTEX
ADRENAL MEDULLA

adrenosterone
progesterone (?)
estrone (?)
(Adrenal sex hormones)

11 - desoxycorticosterone
and Compound S
(Hormones affecting chiefly electrolyte balance)

CORTISONE

[17-hydroxy-11-dehydrocorticosterone]

and/or

Compound F

[17-hydroxycorticosterone]

(Hormones affecting chiefly carbohydrate and protein metabolism.)

EFFECTS ON ABOVE RELATIONSHIPS FOLLOWING PARENTERAL ADMINISTRATION OF

ADRENOCORTICOTROPIC HORMONE	CORTISONE
Depresses secretion of Adrenocorticotropic Hormone by pituitary.	Depresses pituitary Adrenocorticotropic Hormone secretion.
Causes adrenal cortical hypertrophy (reversible when Adrenocorticotropic Hormone injections cease).	Causes adrenal cortical atrophy (reversible when cortisone injections cease).
Stimulates adrenal secretion of cortisone and other cortical hormones provided functioning adrenal cortices are present.	Depresses adrenal cortical secretion. ✓

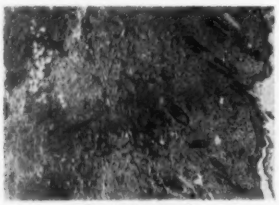
*Cortisone is supplied by Merck and Co., Inc., under the trade-mark name CORTONE.

EFFECT OF CORTISONE ON THE IMMUNE RESPONSE

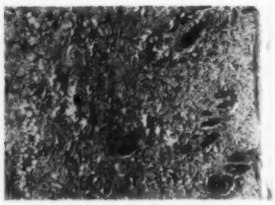
INHIBITION OF KOCH PHENOMENON BY CORTISONE

Guinea pigs previously vaccinated with heat-killed tubercle bacilli.

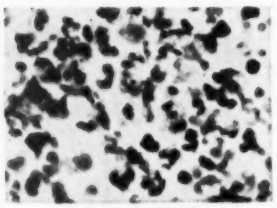
Photographs demonstrate effects 18 hours after the subcutaneous administration of live tubercle bacilli.



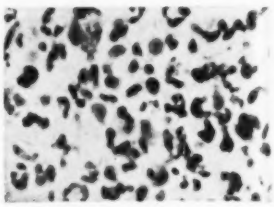
Control animal
Acute inflammatory reaction in dermis and subcutaneous areolar tissue.



Animal treated with cortisone (5 daily inject. of 3 mg.)
Absence of inflammatory reaction.



Control animal
Active phagocytosis of tubercle bacilli.

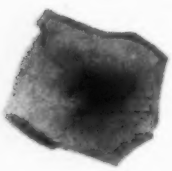


Animal treated with cortisone
Marked decrease in phagocytosis of tubercle bacilli.

INHIBITION OF TUBERCULIN REACTION BY CORTISONE

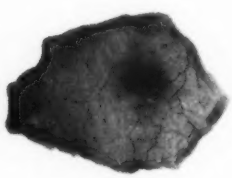
Guinea pigs previously vaccinated with heat-killed tubercle bacilli. .05cc OT injected intracutaneously.

Photographs show tuberculin reaction 24 hours later.



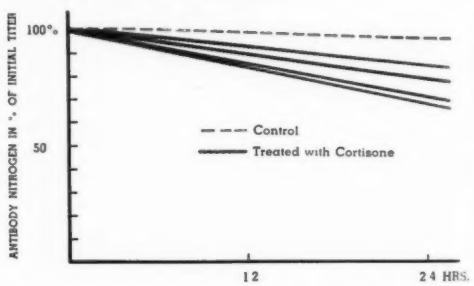
←Control animal. Note extent of reaction.

Animal treated with cortisone (5 daily inject. of 3 mg.). Note marked decrease in extent of reaction. →



EFFECT OF CORTISONE ON ANTIBODY PRODUCTION

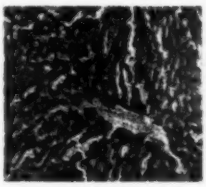
Rabbits immunized previously with crystalline egg albumin. Antibody nitrogen expressed as percent of initial titer drops in animals treated with cortisone as compared to relative maintenance of initial level in non-treated animals.



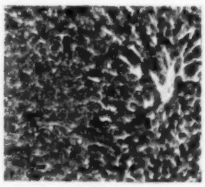
PRINCIPAL METABOLIC EFFECTS OF CORTISONE

CARBOHYDRATE METABOLISM

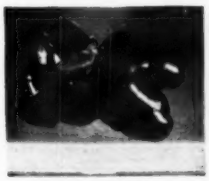
Cortisone → increase in gluconeogenesis → hyperglycemia, glycosuria, insulin resistance, liver glycogen increase



Before



After



Before 85 Gm.

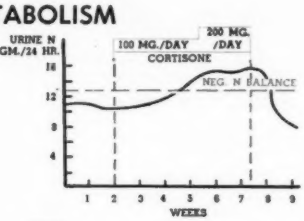
After 175 Gm.

Rabbit livers before and after 6-8 mg./Kg. Cortisone daily for 11 days, demonstrating glycogen deposition.

These changes inconstant in patients not having disturbance of carbohydrate metabolism. Cortisone increases insulin requirement in diabetic patients.

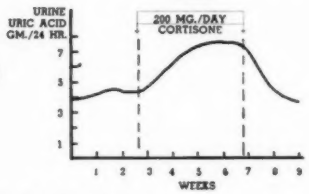
PROTEIN METABOLISM

NITROGEN BALANCE



Cortisone 100 mg./day —little or no effect on nitrogen balance. 200 mg./day—may cause neg. N balance indicative of destruction of N-containing tissue. Retention of N after discontinuance of large doses of cortisone reflects tissue repair.

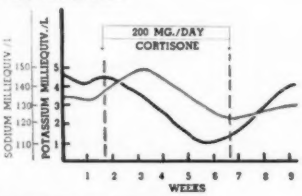
URIC ACID EXCRETION



Increased excretion of uric acid (probably a reflection of nitrogen-containing tissue destruction).

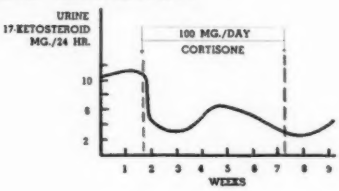
ELECTROLYTE BALANCE

SODIUM AND POTASSIUM PLASMA LEVELS



High dosage of cortisone—serum potassium levels often fall, reflecting increased potassium excretion. Effects on sodium balance are variable; the tendency, however, is for retention of sodium early, followed by increased excretion later in the course of administration of cortisone.

KETOSTEROID EXCRETION



The drop in 17-ketosteroid excretion is due to a depression of steroid hormone production by adrenal cortices. Residual ketosteroid excretion during therapy probably due largely to excretion of metabolic products of cortisone.

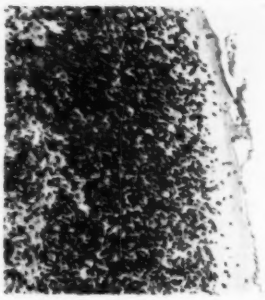
OTHER PHARMACO-PHYSIOLOGIC EFFECTS OF CORTISONE

INVOLUTION OF LYMPHATIC TISSUE

Cortisone causes involution of the thymus, spleen and lymph nodes in the experimental animal.

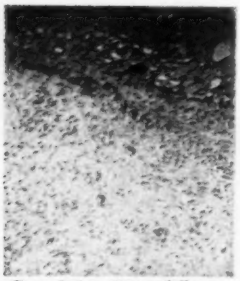
◄Thymus of normal control rat.

Thymus of rat treated with cortisone. Note lymphatic tissue involution. ►

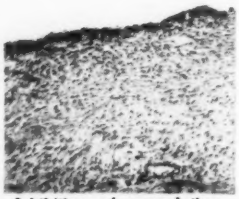


INHIBITION OF REACTIVITY OF CONNECTIVE TISSUE

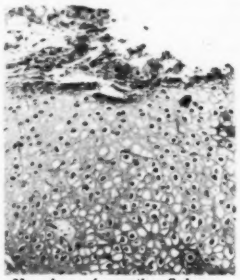
In the normal rabbit, high dosage of cortisone delays the development of granulation tissue in wounds, and new bone formation in fractures. Significance of this finding is unclear—in humans on cortisone therapy, in positive nitrogen balance, prompt healing of decubitus ulcers has been seen, and normal healing of wounds is the rule.



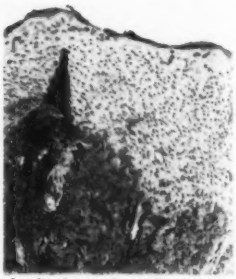
Granulation tissue following wound in untreated rabbit.



Inhibition of granulation tissue in rabbit treated with cortisone.



New bone formation 8 days following fracture in control rabbit.

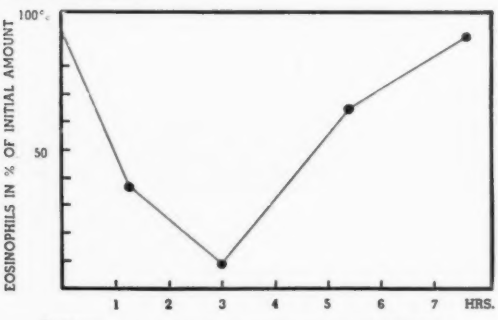


Lack of new bone formation 8 days following fracture in rabbit treated with cortisone.

Charles Rogan, M.D. Dept. of Med. Columbia Univ. College of Physicians & Surgeons

EFFECT ON CIRCULATING EOSINOPHILS

Cortisone causes a temporary drop in circulating eosinophils; possibly by inducing migration into intercellular tissue spaces.



EOSINOPHIL RESPONSE TO CORTISONE IN ADRENALECTOMIZED MOUSE

OTHER HORMONAL EFFECTS

Prolonged administration of large doses of cortisone may induce many of the clinical features of Cushing's Syndrome. These regress after hormone is stopped. Mild to moderate changes in mood have been observed. Acute psychoses have occasionally occurred during administration of cortisone

Cutaneous striae

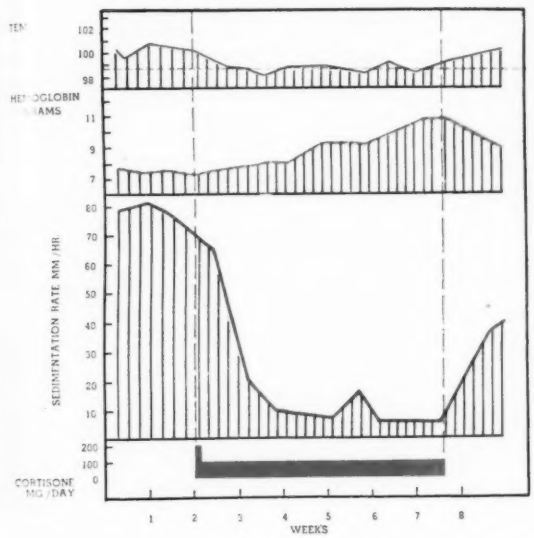
"Moon" facies

From Archives Internal Medicine — February 1950

THERAPY WITH CORTISONE* RHEUMATOID ARTHRITIS

Following Hench, Kendall, Slocumb and Polley's original observations of the ability of cortisone to induce prompt remission of the acute manifestations of rheumatoid arthritis, the dramatic beneficial effect of cortisone in this disease has been consistently reproduced in several hundred patients. Cortisone promptly results in reduction of stiffness, decrease of pain on motion, and loss of tenderness and swelling. While many patients are completely relieved, the average over-all relief is about 85 to 90 per cent as long as treatment is maintained. Manifestations of rheumatic activity usually recur following withdrawal of therapy with cortisone, although in a few cases remissions induced by cortisone have lasted several months.

Female 17 years old: severe rheumatoid arthritis involving practically all joints of the extremities; 5 months' duration.



Synovial biopsy before cortisone. Note severe inflammatory reaction.

Biopsy after 39 days of cortisone. Cellular reaction has changed to fibrous healing.

Male 41 yrs.: severe rheumatoid arthritis 5 yrs.: before cortisone.

Reduction of swelling by cortisone.

Severe rheumatoid arthritis: 4 hours before the first injection of cortisone.

After 8 days of cortisone. Walking normally down stairs without pain or stiffness.

After further therapy, running easily.

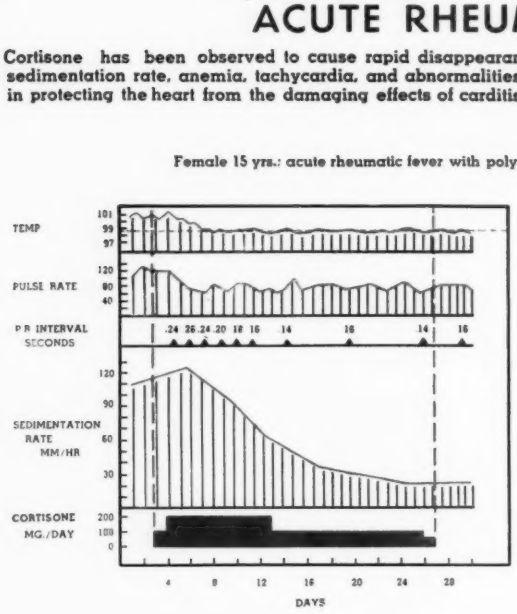
From Archives Internal Medicine — April 1950

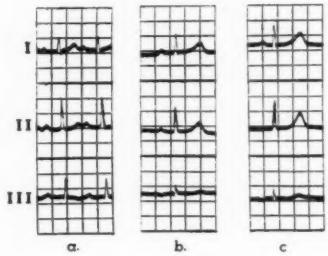
*Cortisone is supplied by Merck and Co., Inc., under the trade-mark name CORTONE.

THERAPY WITH CORTISONE
ACUTE RHEUMATIC FEVER

Cortisone has been observed to cause rapid disappearance of polyarthritis and fever, and to correct elevation of the sedimentation rate, anemia, tachycardia, and abnormalities in the electrocardiogram. The ultimate effect of cortisone in protecting the heart from the damaging effects of carditis will require long-term study for proper evaluation.

Female 15 yrs.: acute rheumatic fever with polyarthritis and carditis 4 days' duration: first attack.





a. Admission ECG P-R int. = .24 sec.

b. After 4 days B with Cortisone, P-R int. = .20:

c. After 8 days B, P-R int. = .16.

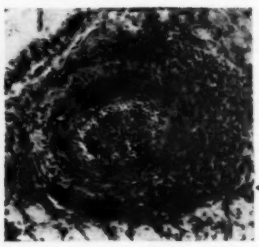
Female 16 yrs., acute rheumatic fever with carditis.

Before Cortisone therapy

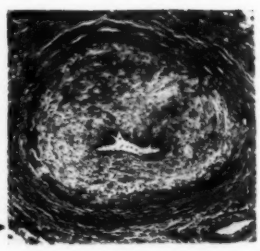
After conclusion of 3 wk period of Cortisone B

One month later

THERAPY WITH CORTISONE
PERIARTERITIS NODOSA



When treated early, encouraging responses have been noted in this disease. When treated late in the course of the disease, the response is poor and patients die of cardiac and/or renal complications secondary to widespread vascular occlusions despite healing of periarteritic lesions.

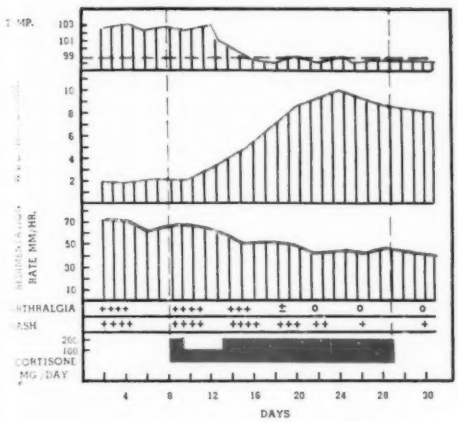


←Before Cortisone. Note perivascular inflammatory reaction.

After Cortisone. Note absence of inflammatory reaction→

THERAPY WITH CORTISONE– ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS

The response varies from case to case. In many patients partial to complete remissions have occurred. Disappearance of fever, arthralgia, and skin rashes, together with correction of pancytopenia and A/G ratio abnormality have been observed. In patients in whom complete symptomatic remissions have been induced, L.E. cells have persisted in many instances, indicating that the disease is probably suppressed rather than cured by cortisone.



←Female 18 yrs.: acute illness 2 weeks. arthralgia several months.

Female
45 yrs.: duration of illness 5 yrs.

←Before therapy with cortisone

After cortisone →

THERAPY WITH CORTISONE – INFLAMMATORY EYE DISEASE

Phlyctenular conjunctivitis, keratitis, iritis, iridocyclitis, uveitis, and sympathetic ophthalmia respond favorably to administration of cortisone. The beneficial results are reported as more prompt and equal to or exceeding responses obtained with traditional methods of therapy. Cortisone has been found effective both when given systemically and when instilled locally as a saline suspension.

ACUTE IRITIS WITH SECONDARY GLAUCOMA

Intramuscular cortisone: total of 1100 mg. over a 5-day period

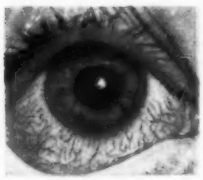
Pretreatment. Vision 20/137
Eyeball tension 48 mm. (Schiotz)

2 hrs. after initial cortisone.
Vision 20/32
Tension 35 mm.

After 21 hrs. cortisone.
Vision 20/20
Tension 20 mm.

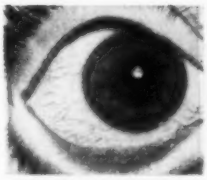
SUPERFICIAL KERATITIS

Topically instilled cortisone; 1 drop 4:1 suspension in eye q. ½ hr. during day and q. 2 hrs. at night.



Pretreatment.

After 2 days' treatment.

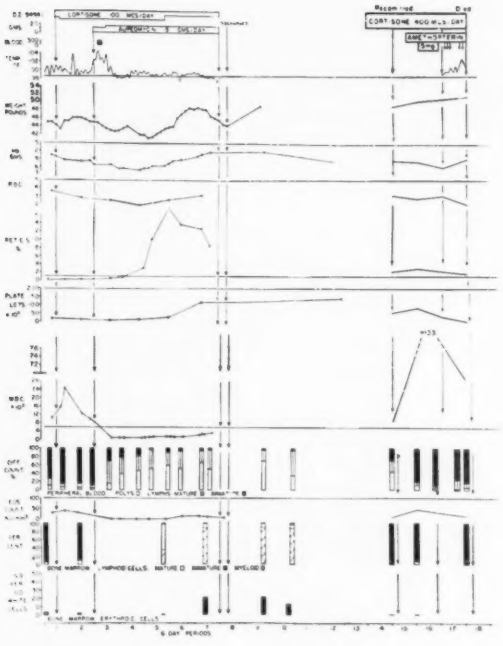


After 3 days treatment.

Illustrated cases courtesy of E. H. Stefteson, M.D., Detroit, Michigan

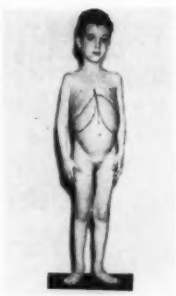
THERAPY WITH CORTISONE – ACUTE LEUKEMIA

Acute leukemia, lymphocytic or granulocytic but not monocytic, responds temporarily to therapy with cortisone. Hematologic and clinical remissions have been induced in some patients. A tendency to refractoriness to subsequent courses of therapy with cortisone has been observed. The effects seen in this disease attributable to cortisone are more important from the standpoint of leading to a better understanding of the nature of the disease than from that of practical therapeutic value. Transient beneficial effects also noted in subacute and chronic lymphatic leukemia.



← Male 4 yrs.: acute lymphocytic leukemia, 6-8 months' duration, at first responded to and then developed resistance to anti-folic acid therapy.

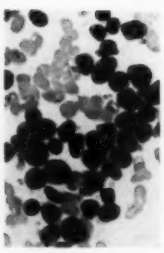
↓



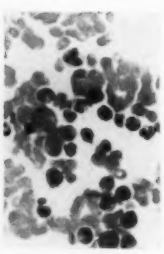
At onset of B with Cortisone

1 month after 5½ weeks of Cortisone

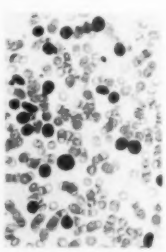
Acute granulocytic leukemia: hematologic and clinical remission induced with 100 mg. cortisone I.M. daily for 20 days.



Bone marrow pretreatment



Bone marrow remission



Peripheral blood pretreatment

Peripheral blood remission

Buffy coat pretreatment

Buffy coat remission

Clinical material courtesy Otto H. Pearson M.D., Leonard P. Lintz M.D., and Rulon W. Rawson M.D. Memorial Center for Cancer and Allied Diseases New York

THE CLINICAL USE OF CORTISONE*

In only a little more than one year cortisone has been used in the treatment of a large variety of diseases, for many of which there has not existed a reliable form of therapy. Hypersensitivity plays a role as an outstanding feature in the pathogenesis of a number of these diseases. The dramatic beneficial effect of cortisone in many of these diseases surpasses effects produced by any previous method of therapy.

RESPONSE IN VARIOUS DISEASES**

BENEFICIAL EFFECT OFTEN DRAMATIC	RESULTS ENCOURAGING BUT REQUIRE FURTHER EVALUATION	TRANSIENT BENEFICIAL EFFECT	NO BENEFICIAL EFFECT
Rheumatoid Arthritis	Pemphigus	Acute Leukemia (Lymphocytic or Granulocytic)	Myasthenia Gravis
Rheumatic Fever	Exfoliative Dermatitis	Multiple Myeloma	Amyotrophic Lateral Sclerosis
Rheumatoid Spondylitis	Acute Gouty Arthritis	Lymphosarcoma	Chronic Myelogenous Leukemia
Still's Disease	Ulcerative Colitis	Hodgkin's Disease	Acute Monocytic Leukemia
Acute Lupus Erythematosus (Early)	Scleroderma (Early)	Chronic Lymphatic Leukemia	Poliomyelitis
Addison's Disease	Dermatomyositis		
Asthma (Status Asthmaticus)	Angioneurotic Edema		
Uveitis, Iridocyclitis, Iritis	Penicillin Hypersensitivity		
Sympathetic Ophthalmia	Periarteritis Nodosa (Early)		
Psoriatic Arthritis			

** The results reported in this chart in certain diseases are preliminary due to the relatively small number of cases treated, uncertainty as to optimum dosage and duration of treatment, and insufficient period of observation following treatment.

*Cortisone is supplied by Merck and Co., Inc., under the trade-mark name CORTONE.

THERAPY WITH CORTISONE – PRECAUTIONS

Undesirable hormonal effects of cortisone may become manifest in certain patients. Careful observations for the development of these effects, plus prompt corrective management of the patient may prevent serious difficulties.

PSYCHIC CHANGES

While definite improvement in mental attitude of patients receiving cortisone usually occurs, in certain instances an exaggerated sense of well-being, and infrequently a manic state may be produced. Mental depression has been reported. In rare instances, pre-existing or latent mental derangement seems to have been intensified or precipitated. The mental changes may occasionally appear during the first few days of therapy. Premonitory signs and symptoms of psychotic reactions occur, such as pronounced swings of mood and insomnia.

Mental changes induced by cortisone do not persist if the drug is promptly stopped. In selecting patients for therapy with cortisone, a careful psychiatric evaluation of the patient's personality and family history should be made, and cortisone not used, or used with caution, if the individual has an unstable personality background.

SODIUM AND WATER RETENTION

Sodium and water retention is a commonly observed hormonal effect of cortisone. It is usually possible to avert these difficulties by maintaining sodium chloride intake at less than 1 gram daily for adults, and proportionately smaller amounts for children.

POTASSIUM DEPLETION

High dosage of cortisone may cause increased urinary excretion of potassium with the production of metabolic alkalosis. Weakness, hypotension, depression of T waves, S-T segment and S-T junction of the electrocardiogram, increase in the CO_2 combining power, and chloride depletion are indications of potassium depletion. If any of these changes occur, dosage with cortisone should be reduced or potassium administered with the hormone.

HYPERGLYCEMIA

Increase in blood sugar and impaired glucose tolerance has been observed in non-diabetic patients during administration of cortisone. In patients with co-existing diabetes mellitus, insulin requirements are usually increased but revert to their original levels soon after discontinuation of the drug.

GENERAL PRACTICE *Review*

To provide the general practitioner, as well as the specialist with concise, readily available information on the latest, proved methods of treatment of conditions commonly encountered in an average practice, POSTGRADUATE MEDICINE *offers this department to its readers. It is not, of course, intended to present these discussions as the only acceptable therapeutic procedures to be used, but rather to offer simple regimens and recommendations based on the extensive experience of the physicians who prepared these summaries.*

Management of Hay Fever

MERLE W. MOORE

PORTLAND, OREGON

Hay fever is a symptom complex characterized by excessive sneezing, a watery nasal discharge, and lacrimation and itching of the eyes and nose. These symptoms recur seasonally in individuals who are allergic to plant pollens.

The most characteristic feature of hay fever is its periodic recurrence. Roughly there are three seasons of hay fever. Trees pollinate from January through April, grasses from May to the middle of July, and weeds through the summer until the first frost. There are some areas, however, such as parts of California and some of the southern states, in which pollination occurs throughout the year. This is particularly true where irrigation is used in warm areas. One should know the clinical flora in the patient's environment and their pollinating seasons to discover the offending pollens

The clinical symptoms of hay fever will be worse when the pollen counts are high. Thus, when the air is dry and windy, severe symptoms may be expected. The season may vary from year to year, depending upon the amount of pollen present.

The clinical diagnosis is generally easy, though it must be differentiated from common colds, vasomotor rhinitis, and acute or chronic sinusitis. The specific diagnosis consists of making skin tests to detect pollens to which the patient is sensitive.

Pollens which are plentiful in the environment and ripe at the time of the attack are selected for skin testing. The choice of methods of skin testing depends upon the experience of the examiner. Scratch testing will show the offending pollens; intracutaneous testing, if used in gradually increasing concentration, will not only determine the offending pollens, but it will also give the degree of sensitivity of the patient and thus help determine the dosage in treatment.

The ophthalmic test may be used to confirm a questionable sensitivity when the skin tests seem doubtful.

The greatest complication of hay fever is asthma. Fifty per cent of untreated hay fever cases will develop asthma. This is frequently preceded by bronchitis which should be a warning. Sinusitis may develop because of continual nasal block. Vasomotor rhinitis, urticaria, eczema, and other allergic manifestations may develop by virtue of lowered allergic thresholds.

The specific treatment consists of giving gradually increasing doses of the specific pollen to which the patient is sensitive. Thus his resistance is built to that particular pollen The pollens selected will be the ones which have shown positive skin reactions and which correspond to his season and are found in his environment.

Unfortunately, there is no set standard for pollen extracts. The extracts are measured by weight, by volume, total nitrogen, protein nitrogen, or molar units. Generally there are three dilutions used, the strongest being one hundred times the

weakest. It does not matter which standard is used as long as the physician is thoroughly familiar with the one he chooses.

Before treatment is started, one must determine the degree of sensitivity of the patient. This can be done by testing with serial dilutions of the pollen extract. If a patient shows a marked reaction to the intermediate solution, he has average sensitivity and if he shows a marked reaction to the strongest solution, he is slightly sensitive.

There are three methods of treatment relating to time. The first and preferable one is prophylactic or pre-seasonal. In this method, treatment is started at least six weeks in advance of the season. The second time method is phylactic or co-seasonal. This is used mostly for patients who come for treatment for the first time during a seasonal attack. Injections must be closely spaced and the results are not as good as in the pre-seasonal method. The third method is the perennial or annual method. In this, the patient receives an injection every few weeks throughout the year in addition to pre-seasonal treatment.

The patient should remain under observation for one-half hour after an injection in order that a constitutional reaction may be observed and epinephrine administered if a reaction develops.

A moderate swelling about the size of a silver dollar, accompanied by redness and itching and lasting six to eight hours is to be expected. It should entirely disappear in twenty-four hours. A constitutional reaction will usually develop within fifteen minutes after an injection. There is itching of the palms and scalp, sneezing, coughing, wheezing, urticaria, and edema. Asthma may be very severe and fatalities have occurred. The sooner the reaction occurs after the injection, the more severe and serious are the symptoms.

Pollen desensitization alone does not give satisfactory relief in every case. There are secondary factors which may be present only during the hay fever season. When the allergic threshold is lowered by virtue of hay fever, other factors such as dust, danders, or other types of inhalants, as well as foods, may act in a secondary manner. If a patient shows a high sensitivity to any of these antigenic factors, other than pollens, they should be included in the desensitization therapy.

The antihistaminic drugs have been of great value with desensitization therapy. They have in no way replaced the injected pollens but they will control the symptoms during the days when the pollen counts are high. The antihistamines should be used as supplementary drugs and not as a replacement for pollen injections.

Generally the prognosis of pollen desensitization is excellent. Most patients respond to three or four seasons' treatment. A few require only one and some need many years of treatment. There is no way to tell in advance the time required for satisfactory results. Patients' abilities to respond vary.

Failures of treatment may be due to faulty selection of pollens, poor judgment of dosage, deteriorated extracts, or failure to recognize factors other than pollens.

Management of Allergic Dermatitis

STEPHAN EPSTEIN

MARSHFIELD CLINIC, MARSHFIELD, WISCONSIN, AND UNIVERSITY OF MINNESOTA MEDICAL SCHOOL, MINNEAPOLIS

For practical purposes, allergic dermatitis or eczema may be divided on a somewhat pathogenic basis as follows:

1. Atopic dermatitis (neurodermatitis).
2. Contact dermatitis.
3. Infectious eczemas (bacterial, mycotic, and other parasitic eczemas), including seborrheic dermatitis.
4. Miscellaneous forms of eczema.

ATOPIC DERMATITIS (NEURODERMATITIS)

The various forms of atopic dermatitis are skin manifestations of a constitutional disorder which also provides the background for bronchial asthma, hay fever, and certain other so-called allergic disturbances.

There is some indication that the new "miracle drugs," the adrenocorticotropic hormone (ACTH)

and cortisone, exact a beneficial effect on some fundamental disorder underlying atopic diseases. Unfortunately, therapeutic results in atopic dermatitis have not been as promising as in hay fever and asthma.

Much more, however, is known about the exciting factors of atopic dermatitis, especially allergic reactions, psychologic and emotional disturbances, and endocrine factors. At present, treatment of atopic dermatitis consists of correcting these disturbances plus adequate local treatment.

As in all chronic diseases other factors, such as secondary infection, may become more prominent as time goes on. Furthermore, repeated and chronic inflammations may lead to irreversible permanent changes of the skin, especially thickening and pigmentation which often are as irreversible as bronchiectasis in the lungs.

Treatment of atopic dermatitis—Treatment has to consider all or some of the following:*

1. Proper topical treatment.
2. Management of pruritus.
3. Allergic factors.
4. Psychologic factors.
5. Endocrine factors.
6. General supportive measures.

1. *The topical treatment of atopic dermatitis* is not very different from that of other forms of eczema and will be discussed more fully under that heading.

2. *Management of pruritus*—Antihistaminic drugs may be tried orally or parenterally. The relief obtained varies from good to zero. In general, the antihistaminics have not lived up to expectations in atopic dermatitis. However, at times, especially in flare-ups, they are very helpful. Topical application of antihistaminic ointments may be tried in the chronic cases; these creams are more effective in the localized form of atopic dermatitis.

3. *Allergic factors* in atopic dermatitis are usually underestimated by the dermatologist and overrated by the allergist. In regard to environmental allergens, such as animal dusts, elimination, if possible, is the preferred method. However, this is not always feasible, especially in cases which show sensitivity to house dust. In these instances desensitization is indicated. Desensitization in atopic dermatitis is at least as difficult and unpredictable as in asthma. Proper dosage can be established only by experience; customarily we start with a 1:1,000,000 dilution. At times this must be diluted even more. Overdosage may produce severe and long-lasting aggravations.

In regard to food allergens, skin tests are usually of no or little help, except in infantile atopic dermatitis. Dietary management is of help in determining food allergies.

4. *Psychologic factors*—This aspect of atopic dermatitis has been overemphasized in recent years. Still, nervous and psychologic factors play an important part in some instances. Many patients with atopic dermatitis are of the hyperactive and of the hyper-reactive type. The nervous tension of these patients is usually apparent; many suffer from hyperhidrosis of the hands and feet.

Psychologic problems play a greater role in the severe generalized cases especially with acute flare-ups involving the face. Often we find those telling "neurotic excoriations." Other cases indicating psychologic conflicts are the circumscribed lichen simplex chronicus.

5. *Endocrine factors*—It is well to remember that there are usually factors other than, or in addition to, psychologic conflicts responsible for localized chronic atopic eczema. Its occurrence around the time of menopause and the male climacteric indicates an endocrine imbalance. In many instances, especially in women, the combination of estrogens and good local therapy, especially antihistaminic creams and x-ray therapy, is very helpful.

CONTACT DERMATITIS

Contact dermatitis, as it is understood generally nowadays, designates cutaneous manifestations caused by surface contact with an excitant. This definition is a broad one and covers actually very different forms of dermatitis. Most commonly, we mean allergic contact dermatitis. But there are instances of nonallergic dermatitis produced by contact with irritating chemicals. Thus we may distinguish in principle between toxic contact dermatitis caused by contacts which will produce dermatitis in almost everybody, and allergic contact dermatitis where the excitant produces the dermatitis only in sensitized people.

ALLERGIC CONTACT DERMATITIS

Although the allergic nature of this form of contact dermatitis has been recognized for a long time, the mechanism is still not fully understood. Contact dermatitis is provoked by so-called simple chemicals such as inorganic compounds or aniline dyes, in contrast to the highly complex protein allergens encountered in atopic diseases.

The allergen in contact dermatitis reaches the skin normally by external contact, hence the name; it may also reach the skin from within.

The allergens may be solid, liquid, volatile substances, or even gases or fumes. Solids and fumes usually produce a contact dermatitis at the site of direct contact. With liquids, the dermatitis appears

*For a more detailed description of the treatment of atopic dermatitis the reader is referred to the bibliography at the end of this discussion.

often first or exclusively on other parts of the body where it is carried by contaminated fingers; for instance a dermatitis from turpentine may show up first on the scrotum.

Repeated attacks of contact dermatitis tend to produce severe and long-lasting sieges of contact dermatitis, which may require many months of treatment. When this stage has been reached, elimination of the causative factor alone is not sufficient to yield a cure. This is often seen in industrial dermatitis, especially after it has recurred several times. At this stage the contact dermatitis may persist for weeks or months, even after the worker has quit his job and avoids all contact with the causative factor. Insurance adjusters are prone to conclude that such a dermatitis cannot be of occupational origin. This is an error.

"Industrial dermatitis" also includes a number of other conditions. It is also well to remember that not all cases of contact dermatitis in workmen are occupational. They may be caused by outside or home contacts. Take as an example the dermatitis in a worker due to painting his new house; or the female war worker's dermatitis of the hands which was not caused by contact with metals, but by some cleaning agent used at home.

Even if the dermatitis is of occupational origin, it need not be an allergic contact dermatitis. There are cases of dermatitis caused by primary, nonallergic irritation from strong chemicals. Infections and infectious eczemas also cause, at times, occupational dermatitis.

The diagnosis of a contact dermatitis is largely made by the history, clinical appearance, location, and patch tests.* In eliciting the cause it is helpful to have lists† which contain the most common offenders for the various locations. By checking these lists, the patient may become conscious of contacts of which he was not aware.

Causative treatment of contact dermatitis consists of finding and avoiding the culpable contact. Desensitization is not practical except in certain cases of plant dermatitis, especially from poison ivy and weeds. Where exposure to these plants cannot be avoided, we try oral desensitization with oily solutions of the oleoresins. Of course, this treatment should be started only after the dermatitis has cleared up, or at least subsided considerably. For the prevention of poison ivy dermatitis, injections with a poison ivy extract seem to be helpful in some cases. Usually three or four injections of the commercial extracts at weekly intervals are given early in the year. In very sensitive cases one must start with a small dose, 0.1 cc. or even less. However, *the practice of injecting poison ivy extracts during the acute phase of the dermatitis should be abandoned. This method often severely aggravates the condition in patients who are highly sensitive.*

The symptomatic treatment consists of relieving the skin irritation and the accompanying pruritus and other discomfort. The local and systemic treatment of contact dermatitis is not much different from that used in other forms of dermatitis and will be discussed under infectious eczema.

Where local applications do not suffice to relieve the pruritus, antihistaminics, sedatives, calcium gluconate, or Calcibronat intravenously may be tried. The value of antihistaminics in contact dermatitis is much overrated. Large amounts relieve the pruritus in cases that are accompanied by swelling or urticaria, especially in poison ivy dermatitis. Where oral medication with antihistaminics fails, their parenteral use (especially benadryl, given intravenously) may be helpful. Codeine and demerol are at times of great value in relieving severe pruritus. But one must be careful not to "dope" the patient too much and must be on the lookout for drug sensitivity.

Psychotherapy is of great help. One should point out to the patient the harmlessness of the condition and relieve his fear of a contagious or serious disease. When the patient is still in the eruptive stage, he should be forewarned about further spreading of eruption. Conversely when the dermatitis has reached its peak we may relieve his mind by telling him the worst is over. A patient with a dermatitis, who knows about what to expect, is much more cooperative and patient, qualities which are badly needed in severe and prolonged cases of contact dermatitis.

INFECTIOUS ECZEMA

In a general way we may say that an infectious eczema is due to a combination of an infection and an eczema. This association may occur in different ways:

1. Infection of the skin may lead to an eczematous sensitization to the causative organism. This corresponds to the classical concept of infectious eczematoid dermatitis.

2. An infectious process of the skin may become complicated by a secondary dermatitis of a different nature, for instance a contact dermatitis.

3. An eczematoid dermatitis may become complicated by secondary infection.

4. Infectious eczemas may be complicated by various forms of sensitization, such as bacterial,

*A thorough discussion of the patch test methods including a table listing the nonirritating concentrations of common chemicals, will be found in Sulzberger and Baer: Skin tests and other immunologic procedures in common dermatologic and venereal conditions. Part I. Yearbook of Dermatology and Syphilology, 1943, pp. 7-47. Chicago, The Year Book Publishers, Inc.

†Space does not permit publishing these lists here. The author will be glad to furnish a copy of the charts he uses in his practice, upon request.

contact, or autosensitization. This may lead to an "id"-like generalized eruption.

Such a concept is a broad one and covers a lot more than the conventional term of infectious eczematoid dermatitis. I am overemphasizing the role of infection in eczemas because it is so important, for the proper therapy, to recognize the infectious factor in the various forms of eczema.

The most common forms of infectious eczema are perhaps the following:

1. Acute weeping dermatitis around an infection of the skin, a draining sinus, or following an injury.
2. Eczema of the ears and behind the ears. In this case, the infection may develop secondarily to a contact dermatitis from metal bows of glasses.
3. Infectious eczema of the lower legs, originating from a stasis dermatitis, a varicose ulcer, or a lichen simplex chronicus, with or without "id"-like generalized eruption.
4. Infectious eczemas of the hands.
5. Infected contact dermatitis.
6. Infected infantile eczema.

TREATMENT OF INFECTIOUS ECZEMA

The principles governing the treatment of infectious eczemas are:

1. *Evaluation of factors*—It is important to size up the case. In some instances the infection seems to be the main factor and just the application of an antiseptic is all that may be needed. In other cases, things are very complicated and many different avenues of approach have to be used at the same time.

2. *Local treatment of infection and eczema*—Local treatment of infectious eczema means essentially a combination of an antiseptic against the infection and a preparation against the eczema. *In the acute stage, we must first take care of the infection.*

Acute cases—"Wet treatment"—Compresses with potassium permanganate, 1:6,000; or silver nitrate 1:2,000. After the infection has subsided we use aluminum acetate in the form of Domboro tablets or powders, one dissolved in one quart of water.

"Dry treatment"—A "zinc oil" with an antiseptic.

The formula for an ichthyol zinc oil is as follows:

Ichthyol	2.4 gm.
Boric acid	2.4 gm.
Zinc oxide	48.0 gm.
Corn oil q.s.	120 cc.

Be sure the oil is added to make the volume up to 120 cc. Then the mixture will be a heavy oily suspension.

The antiseptic I prefer is Rivanol ½ to 1 per cent. Other antiseptics that may be added are ammoniated mercury 3 per cent or Zephiran, 0.5 per cent as follows:

Zephiran solution (12 per cent) ..... 5.0 cc.
Ichthyol zinc oil (formula as given) q.s. 120.0 cc.

Apply and bandage two or three times a day.

In my experience zephiran is well tolerated; but it is claimed that it may occasionally have a necrotizing effect. One per cent aqueous gentian violet solution, applied once or twice a day is very effective in acute infectious eczema but also messy.

Subacute stage—The same zinc oils may be used; later on, 2 per cent Vioform vaseline or 3 to 5 per cent ammoniated mercury in zinc oxide ointment.

Chronic stage—3 to 5 per cent coal tar in zinc oxide ointment with the addition of 1 per cent rivanol or 3 per cent ammoniated mercury; or 2 per cent vioform in equal parts of Wilkinson's ointment (Ung. sulfur compos. U.S.P.) and boric acid ointment.

Infectious eczema of the hands (subacute to chronic stage)—Vioform 0.6, dernaftan 1.5, castor oil 3.0, Lassar's paste, Ung. acid boric aa. q.s. 30.0.

Dry infectious eczema of the ears, also mild eczema of the face with folliculitis—Bacitracin cream q.i.d. or still better, aureomycin cream q.i.d.

Infected lichen simplex chronicus—3 to 5 per cent ammoniated mercury ointment or any of the ointments mentioned for the chronic stage. For the nape of the neck and scalp, only subacute or chronic stage: histadyl cream (5 per cent) 5.0, bacitracin cream aa. 15.0. Apply q.i.d.

Here are a few general remarks:

People suffering from infectious eczemas are more easily sensitized to medication than any other group. Most antiseptics are sensitizers. *Watch out for sensitization.*

Medication must be appropriate for the stage of the dermatitis. Do not use a strong ointment during the acute phase; do not apply a washable cream to a weeping dermatitis.

Do not overtreat. If your treatment is not immediately successful, do not change constantly to different medications. Try to stick to a few tested preparations which have a low sensitizing index. Do not use penicillin as an ointment. Try to avoid furacin and sulfonamides, topically. Apply your antiseptic ointment only to the area where there is actual infection. In generalized eruptions, the "id"-like rash accompanying the infectious eczema is purely allergic and not infectious. This eruption usually requires only mild local treatment.

3. *Systemic treatment of infection*—Penicillin is preferred unless there is a history of penicillin sensitivity. In this case, we use triple sulfonamides 1 gm. q.i.d., later less. Trial with aureomycin or chloromycetin is indicated in resistant cases.

4. *Correction of contributing factors* (contact

sensitivities, food or environmental allergies, anemia, impaired circulation, diabetes).

5. *Supportive therapy* (vitamins, liver extract, proteins, ultraviolet irradiation).

6. *Psychosomatic approach.* Such factors are encountered mostly in cases combined with atopic eczemas.

7. *Removal of foci of infection*—One must wait until the eczema is under control. The patient should receive adequate amounts of penicillin or sulfonamides, at least twenty-four hours *before* the removal, and for three to seven days afterwards, depending on the severity of the infection.

8. *Desensitization should be reserved for persistent cases.* Each case must be individualized. Selection of the vaccine (we use stock vaccine) and dosage are guided by the patient's skin reactions. I start with rather weak dilutions, usually 1:10,000 or less. If subcutaneous injections produce flare-ups, one may try the intradermal method.

9. *Nonspecific therapy*—If all these methods fail, or perhaps even sooner, we should remember the old fashioned nonspecific therapy. The mildest is perhaps Proteolac, but probably also least effective. Another milk derivative, Aolan, is more effective but may produce more reactions. Typhoid fever therapy should be reserved for the most stubborn cases.

OTHER FORMS OF ALLERGIC DERMATITIS

There are many cases of eczema that do not fit the three categories discussed in this paper. We must realize that an eczema represents often a combination of various factors and forms, and we must also realize that our etiologic and pathogenetic knowledge is rather limited. However, the application of the principles presented should be of help in the approach to most forms of eczema.

REFERENCES

Epstein, Stephan: Atopic dermatitis (Graduate instructional course in allergy, American College of Allergists, Cincinnati, November 3-8, 1947).

———: Management of dermatitis in general practice. Wisconsin M. J. 46:707-715 (July) 1947.

Lewis, George M., and Cormia, Frank E.: Office management of the neurodermatoses. New York State J. Med. 47:1889-1894 (September) 1947.

Lynch, F. W., Hinckley, R. S., and Cowan, D. W.: Psychosomatic studies in dermatology; psychobiologic studies of patients with atopic eczema. Arch. Dermat. & Syph. 51:251-260 (April) 1945.

Macaulay, W. L.: Industrial dermatitis. Am. Practitioner 2:11-15 (September) 1947.

Randolf, Theron: Adrenocorticotropic hormone (ACTH), its effects in bronchial asthma and other allergic conditions. Annual Congress, American College of Allergists, St. Louis, January 16, 1950.

Rostenberg, Adolph, Jr.: Eczematous sensitization. Arch. Dermat. & Syph 56:222-232 (August) 1947.

Rostenberg, Adolph, Jr.: Immunologic concepts which underlie atopic dermatitis. Symposium on Allergy, American Academy of Dermatology, Chicago, December, 1947.

Simon, F. A.: A study of atopic eczema. Ann. Allergy 6:584 (September-October) 1948.

Sulzberger, M. B.: Dermatologic Allergy. Springfield, Ill., Charles C Thomas, 1940.

Urbach and Gottlieb: Allergy. Ed. 2. New York, Grune & Stratton, 1946.

Walsh, M. N., and Kierland, R. S.: Psychotherapy in the treatment of neurodermatitis. Proc. Staff Meet., Mayo Clin. 22:578-584 (December 10) 1947.

Weedon, F. R.: Quoted from Epstein and Macaulay: Allergic skin diseases. Ann. Allergy 6:442-479, 1948 (p. 443).

Treatment of Bronchial Asthma

J. WARRICK THOMAS

THE THOMAS CLINIC; MEDICAL COLLEGE OF VIRGINIA, RICHMOND

In true allergic bronchial asthma, as differentiated from other nonallergic asthmas, the attacks are precipitated by a reflex mechanism resulting from exposure to an allergen either by inhalation, ingestion, parenteral administration, or absorption of bacterial allergens from a focus of infection.

This discussion will be limited to a consideration of the treatment of bronchial asthma, and complications of bronchial asthma will be considered only superficially.

CLASSIFICATION

Asthma in general may be classified as (1) nonallergic asthma[1] (cardiac, obstructive and thymic), and (2) allergic asthma, including (a) extrinsic, or noninfective[2] asthma due to inhalants including pollens, molds, etc., ingestants, injectants, drugs, etc.; (b) intrinsic asthma due to a bacterial allergy, and (c) a combined extrinsic and intrinsic asthma, including status asthmaticus, or the severe and pro-

longed asthma that has not responded to the usual methods of treatment.

TREATMENT

Asthma therapy must be considered from the point of view of simple bronchial asthma and bronchial asthma accompanied by complications such as emphysema, bronchiectasis, massive collapse of the lung, periarteritis nodosa, lung abscesses, tuberculosis, etc., which must be treated in conjunction with the recognized therapy of bronchial asthma.

Specific treatment includes avoidance or elimination of the offending agent or substance to which the patient is known to be allergic or which is suspected of causing trouble. Inhalants, including dust, feathers, epidermals, molds, pollens, occupational contacts, etc., ought to be eliminated in so far as possible. Air filtering and air conditioning are of value in certain occupations and for pollen-sensitive patients, especially.

Foods which cause reaction, as determined by history or sensitization studies, whether individually or in combination, should be restricted temporarily and added back to the diet by trial test over a period of several days and retained in the diet if tolerated. Diet lists are important and elimination diets may be tried recurrently. Food diaries assist in determining additional food offenders.

Hyposensitization is indicated when complete avoidance does not control the symptoms. The allergens considered include inhalants, molds, pollens, epidermals, and autogenous vaccines. Rarely do we consider milk and egg hyposensitization orally; however, wheat and certain cereal grains may be tried cautiously hypodermically as well as orally. Methods of hyposensitization with pollens include preseasonal, perennial, and coseasonal treatment. Schedules must be followed carefully and modified according to the patient's tolerance, response to treatment, when there is too long a lapse of time between injections, and after reactions.

Reactions are divided into immediate or delayed types. Delayed reactions require a reduction of dosage. Immediate or constitutional reactions require application of a tourniquet proximal to the site of injection, epinephrine, 0.1 to 0.2 cc. into the site of injection, and dosages of 0.1 cc. up to 1.0 cc. administered in the opposite arm. Varying dosages may be repeated at few-minute intervals depending upon the signs and symptoms of the patient. Intravenous or intracardial injections of epinephrine are rarely necessary. When anoxemia is evident, oxygen therapy is mandatory.

Certain allergens as fungi, cottonseed, horse serum, various epidermals and occasionally pollens must be recognized as extremely potent allergens in certain individuals. Very sensitive cases must be started with extremely dilute extracts, in some instances up to one million or one hundred million, down to more concentrated preparations with a cautious increase of dosage, depending upon the patient's tolerance.

Autogenous extracts are often of proved value when stock extracts or stock vaccines are ineffective in the management of specific therapy.

Nonspecific treatment in acute asthma includes epinephrine or adrenalin 1/1,000, in dosages of 0.2 to 1.0 cc. hypodermically, or epinephrine, 1/100, by aerosol in adequate doses for the relief of symptoms, avoiding an adrenalin reaction. Repeated dosages of both of these preparations after five minutes may be of value in the case of smaller dosages given subcutaneously if the patient does not definitely respond to the therapy. In moderately severe and severe cases, epinephrine in oil intramuscularly in dosages of 0.5 to 1.0 cc. is of value.

Ephedrine, racephedrine, including propadrine and neosynephrine may be considered orally in dosages of ⅜ to ¾ gr. at intervals of three to four hours. The above measures are satisfactorily employed in mild cases.

Aminophylline[3] in dosages of 3¾ to 7½ gr. may be employed intravenously, very slowly, or intramuscularly, usually in combination with procaine, or per rectum in the form of suppository alone, or in combination with pentobarbital sodium; or aminophylline tablets, 3 gr., dissolved in amounts of 3¾ to 9 gr. in water individually or in combination with pentobarbital sodium given as retention enema.

Severe bronchial asthma including status asthmaticus warrants further consideration. Frequently hospitalization[4] is necessary, preferably in a private room in a controlled environment, more or less completely eliminating the common allergens such as dust, feathers, flowers, whether or not the patient is known to be sensitive to them. Dustproof encasings over mattresses and pillows or use of rubber foam mattress or pillows is necessary. Cleanliness of the room is accomplished by use of a damp mop or cloth employing tap water and avoiding strong disinfectants, and the use of volatile oils. Air conditioning and pollen filters may be required although a physical allergy must be recognized if present. Avoidance of drafts and availability of drugs, facilities, and trained personnel facilitate the handling of the patient.

In psychotherapy, unnecessary conversation and over-solicitation of family and friends are discouraged. Quietness, reassurance, confidence, and complete rest as well as the maintenance of an allergic equilibrium are important. Competent nursing and house staff assistance are imperative, and private rather than ward environment is preferred.

Oxygen may be administered by tent, 8 to 14 liters per minute, by mask, either open or closed type, nasal catheter, or hood depending upon the

amount of anoxemia and at a temperature that is satisfactory to the individual case. A tent also helps to establish a nonallergenic environment. Helium and oxygen in combination (20 per cent oxygen, 80 per cent helium) is more effective than oxygen alone in certain cases.

Ether in oil—equal parts of anesthesia ether and oil (sweet oil, cottonseed oil, mineral oil, olive oil)—offers additional means of relaxation to the severely ill asthmatic patient. Dosages vary from 5 to 7 ounces in the average adult; ½ to 2 ounces in children, as retention enema. Have re-breathing tube available as needed.

Avertin as rectal anesthesia may be given in dosages ranging from 60 to 90 mg. per kilogram of body weight administered preferably by an anesthetist and having available coramine and other stimulants to counteract the effects of overdosage. This drug has a narrow margin of safety.

Aminophylline should be tried intravenously, orally, intramuscularly, or per rectum in dosages of 1½ to 9 gr., always administered very slowly, avoiding extravasation (see above for detailed information on aminophylline dosage and administration). Nausea, vomiting, dizziness, faintness, and sensation of heat over body are indications of toxicity, too rapid administration, or overdosage.

Amyl nitrite may be of definite value in bronchial musculature relaxation in the form of inhalation of perle broken in a sponge.

Glucose in saline or glucose in distilled water is employed as a means of maintaining an optimum state of fluid balance, to improve the caloric intake when water and food cannot be taken by mouth. It may be administered in either 5 or 10 per cent dilution in the amount of 500 to 1,000 cc., administered alone or as a vehicle for intravenous epinephrine, 1/1,000, 0.5 to 1 cc., or as a vehicle for other medication such as sodium iodide, vitamin preparations, aminophylline, etc. Fifty cubic centimeters of 50 per cent glucose, either in saline or in distilled water, with or without epinephrine, intravenously, at times will lessen bronchial secretion and relieve the patient of some tenacious mucus.

Opiates[5] are usually discouraged, with the possible exception of demerol in dosages of 50 to 100 mg., and occasionally codeine, as there is a depression of the respiratory center and inhibition of the cough reflex. Morphine should not be given as deaths have been reported[6] from such administration on occasions.

Isuprel sublingually is given in dosages of 5 to 25 mg. depending upon the age, previous administration, and tolerance of the patient. This drug may also be given as Isuprel aerosol, 1/200. Care should be exercised in the avoidance of swallowing of the drug and the mouth should be rinsed after aerosol, as with epinephrine aerosol.

Norisodrine Sulfate (Abbott's) may be administered by an Abbott Aerohalor in cartridges of 10 or 25 per cent powder. This should be inhaled cautiously in the beginning with the 10 per cent powder until a dosage can be established. This at times will relieve asthma when adrenalin does not. It may be longer lasting and produce less side effects. It is worthy of consideration in cases which are moderately severe.

Bronchoscopic examination[7] is occasionally a lifesaving measure to remove plugs of mucus and thus facilitate better aeration. It is carried out with or without local anesthesia; one should exercise caution in the type of local anesthetic used, considering the possibility of drug intolerance.

MISCELLANEOUS MEASURES

Sedatives may include the various barbituric acid group of drugs, pentobarbital sodium, nembutal, seconal, sodium amytal, sodium phenobarbital, etc. Chloral hydrate, 10 to 15 gr. per se or in combination with sodium bromide, 15 to 30 gr., at three- to four-hour intervals when awake or p.r.n. is an excellent sedative. Paraldehyde, orally, per rectum (in oil), or intramuscularly in dosages of 2 to 10 cc. will at times relax the patient when other methods fail. Intravenous alcohol and procaine are of limited value.

As expectorants, the following are worthy of consideration: potassium iodide, saturated solution, 3 to 40 drops well diluted in water three times a day as tolerated; sodium iodide, 15 to 100 gr. intravenously (gradual build-up dosage used when large dosage administered); ammonium chloride enseals, preferably 7½ gr., 2 tablets every four hours.

Antihistaminic drugs are of some value particularly if there is a complicated rhinitis or excessive amount of mucus. The tolerance of individuals is variable; some patients will tolerate one preparation and not another. Antihistaminics may be taken in elixir, tablet, or capsule form in dosages varying from 2 to 100 mg. depending upon the preparation used, the tolerance of the patient, and the relief obtained.

Antibiotics are warranted when infection is present. The following may be used individually or in combination: sulfonamides, streptomycin, aureomycin, chloromycetin, and penicillin (crystalline, aqueous, in dosages of 300,000 to 800,000 units daily preferred). Caution: Do not use oil or beeswax slow penicillin.

As stimulants, caffeine and coramine are employed in dosages and frequencies depending upon the circumstances.

Vitamins offer support either intramuscularly, intravenously, or orally when there is no evidence of sensitization.

Digitalis is contraindicated unless there is evidence of cardiac decompensation.

Aspirin is a useful drug unless an intolerance to the drug is known.

Fowler's solution is of questionable value and toxic reaction or poisoning must be kept in mind.

Blood plasma and transfusions are indicated in debilitated or anemic patients and reaction may be expected.

Nasal surgery is contraindicated in acute and severe asthma unless severe pansinusitis with fever warrants such measures. Polypectomies are deferred until acute phases have subsided. Chest surgery to sympathetic and vagus nerves is of controversial value.

Abscessed teeth, peritonsillar abscesses, acute sinusitis, or other foci of infection should be either drained or excised and one should consider antibiotic therapy in conjunction with such treatment.

ACTH therapy is of potential value but too new and of limited use only in experienced hands due to lack of adequate, prolonged, and proved trial.

Climatotherapy is worthy of consideration after acute or emergency measures have been employed and the patient is in a state of health that will permit travel. Consideration of air travel is usually preferable.

One should exclude doubtful or controversial measures as follows: ethylene disulfonate; histamine diphosphate (intravenously, subcutaneously); x-ray and radium therapy (controversial in acute phase); histaminase or hapamine; intravenous barbiturates including pentothal sodium; autohemotherapy; intramuscular milk injections, and splenic extract preparations.

CONCLUSION

The treatment of bronchial asthma, as evidenced by the preceding discussion, is quite variable and one observes patients to respond favorably on certain treatment that is of possibly limited value when subsequently employed. However, when a patient is allergic and nonspecific measures initially do not control the symptoms, we have to look toward different and varied approaches to relieve the patient. The future of therapy with the many new discoveries of drugs encourages us in considering the subsequent handling of asthmatics; however, caution must be exercised, as frequently there are untoward reactions or side effects which make the treatment worse than the disease.

REFERENCES

1. Thomas, J. W.: Allergy in Clinical Practice. Philadelphia, J. B. Lippincott Co., 1941, p. 112.
2. Cook, Robert A.: Allergy in Theory and Practice. Philadelphia, W. B. Saunders Company, 1947, p. 100.
3. Barach, A. L.: Rectal instillation of aminophylline in intractable asthma. J.A.M.A. 128:589 (June 23) 1945.
4. Thomas, J. W.: The treatment of certain allergic manifestations in medical emergencies. Ohio State M. J. 36:372 (April) 1940.
5. Lamson, R. W., and Butt, E. M.: Fatal asthma; clinical and pathological consideration of 187 cases. J.A.M.A. 109:1843 (May 29) 1937.
6. Vaughan, W. T., and Graham, W. R.: Death from asthma; a warning. J.A.M.A. 119:556 (June 13) 1942.
7. Thomas, J. W., and Fenton, M. M.: Fatalities and constitutional reactions following the use of pontocaine. J. Allergy 14:145 (January) 1943.

COMING POSTGRADUATE COURSES IN ALLERGY

Cook County Graduate School of Medicine, Chicago, Illinois
One month personal course in allergy, first Monday of every month, full time
Six month personal course in allergy, by appointment, full time

University of Illinois College of Medicine, Chicago, Illinois
Postgraduate course in allergy, 12 months, full time, October, 1950

American College of Allergists, Minneapolis, Minnesota
Psychotherapy for allergists, full time, November 6-10, at Psychoanalytic Clinic, Columbia University, New York

University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania
Allergy—clinical and laboratory, full time, October 16-28, at Montefiore Hospital, Pittsburgh, and U. S. Veterans Hospital, Aspinwall, Pennsylvania

Joint Committee on Postgraduate Education, Brooklyn, New York
Allergy, 10 weeks, part time, October, 1950, at Beth El Hospital
Allergy, 8 weeks, part time, October, 1950, at Beth El Hospital
Applied immunologic procedures in children, 8 weeks, part time, October, 1950, at Kings County Hospital

American College of Physicians, Philadelphia, Pennsylvania
Clinical allergy, full time, October 23-November 3, at Roosevelt Hospital, New York

Columbia University, New York, New York
Medicine PM 36 allergy, part time, November 27-December 11, at Mt. Sinai Hospital

New York University Postgraduate Medical School, New York, New York
Allergy 5415-A, 3 weeks, full time, October 16-November 3, 1950
Allergy 543-A, 8 sessions, part time, January 5-February 23, 1951

CORRECTION

Dr. Rufus S. Reeves, author of the article, "Diagnosis and Treatment of Infectious Hepatitis" (*Postgraduate Medicine*, page 410, June, 1950), has requested the Editors to make the following correction relative to the use of Gamma Globulin (page 415): "The accepted dosage is 0.5 cc. per pound of body weight—rather than 2 cc. as stated."

Scientific Exhibit

Intrinsic Asthma

FRANCIS M. RACKEMANN,[1] M.D., WALTER S. BURRAGE,[2] M.D., AND JOHN W. IRWIN,[3] M.D.

ALLERGY CLINIC AND LABORATORY, MASSACHUSETTS GENERAL HOSPITAL, BOSTON

THE adjective "intrinsic" means that the cause of asthma is something which the patient carries with him. This type of asthma occurs in older people, with an onset usually after age 40. (Figure 1.)

Positive skin tests are not uncommon, but evidently have little to do with the cause of trouble: they do not make sense with the present history: some are referable to a clinical sensitiveness in the past. Nasal polyps are more common than in asthmatic bronchitis.

The symptoms continue without regard to changes in season or environment, and this indicates that the trouble is something inside the patient (intrinsic) and not outside the patient (extrinsic), as in the younger patients who are allergic to a dust or food.

ETIOLOGY

Asthma develops only in patients who are predisposed, who have inherited the asthmatic state. In such people, somatic factors such as respiratory or focal infections, the menopause, or merely chronic fatigue with loss of weight are causative. In others, psychic factors seem sufficient to explain the trouble. Mixed causes are almost the rule.

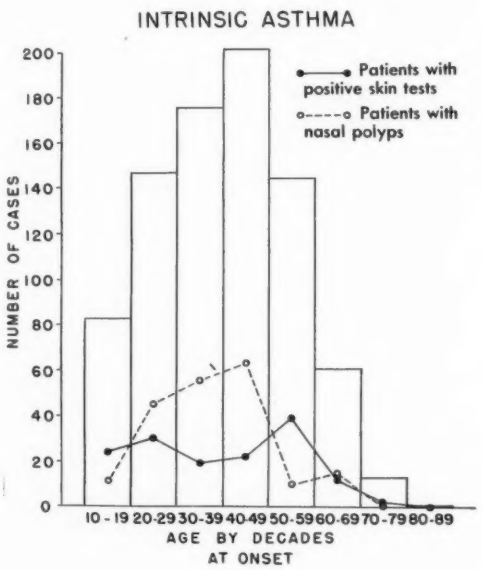


Figure 1

[1]*Board of Consultation, Massachusetts General Hospital;* [2]*Assistant Physician, Massachusetts General Hospital;* [3]*Graduate Assistant in Medicine, Massachusetts General Hospital.*

AGE AT ONSET

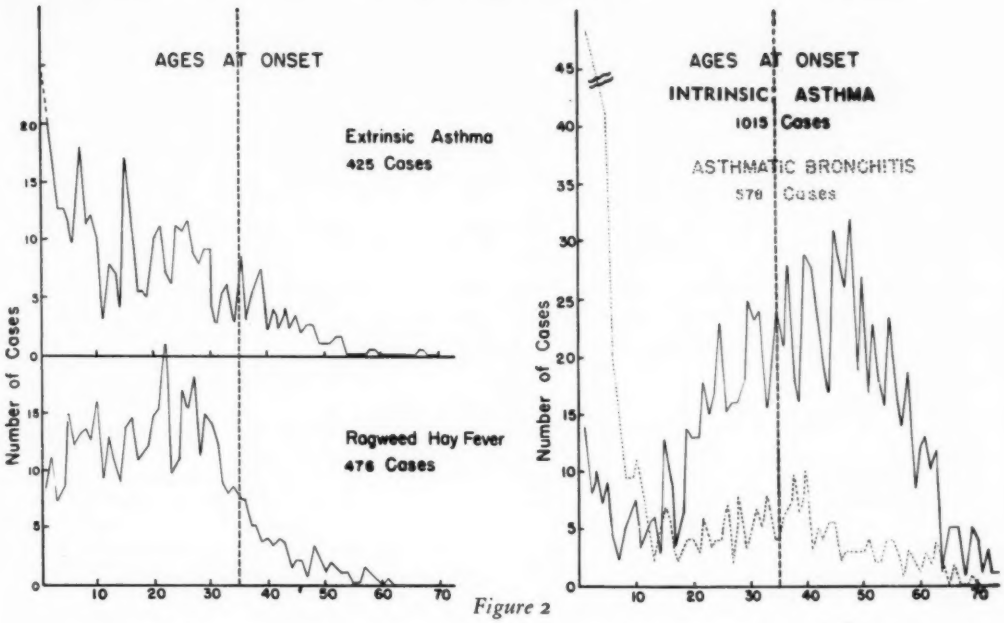


Figure 2

CLASSIFICATION OF ASTHMA

Great stress is laid upon the age at onset, and charts (Figure 2, above) show clearly the age differences between extrinsic asthma due to allergy, and intrinsic asthma dependent upon a cause inside the patient himself.

The age at onset of symptoms is of great practical importance in the clinic. In the left-hand section of Figure 2 (Extrinsic) the upper curve showing the number of cases with an onset of symptoms in each year of age is derived from 425 cases in which the cause of trouble was proved by history and end result to be dependent upon dust and/or food factors. It is most interesting to see that this curve has almost the same shape as the curve for 476 cases of Ragweed hay fever. To see both curves drop off after age 35 is important. In contrast, the intrinsic cases on the right begin at a much later age. Asthmatic bronchitis is treated separately, for it is intermediate between the two more typical groups.

WORKING CLASSIFICATION OF ASTHMA

Asthma Begins Before Age 30	*Asthma Begins After Age 40*
EXTRINSIC (Allergy)	INTRINSIC
Simple—diagnosis easy by history	Bacterial allergy (hard to prove)
Complicated by } infection / depletion	Depletion
Asthmatic bronchitis	Psychic—fatigue, etc.
V.M.R. leads to asthma—often severe	Somatic infections—sinuses, teeth, bronchi, other
	Malnutrition
	(Note Selye's Adaptation Syndrome)
	Polypoid sinusitis
	Emphysema } functional / structural
	Tumors

The Working Classification at the bottom of the previous page is of great practical importance. It is based on the clinical study of patients—especially on the history. It includes a number of typical cases.

TYPICAL CASES

- The "spoiled child"
- Asthmatic bronchitis—common in young adults
- The "tired business man"—sudden asthma at age 45
- The "harassed housewife"—attacks at first, persistent later
- The older man or woman—emphysema (or rarely, a tumor)

The spoiled child may be allergic, but in some cases relief in the hospital is due not to escape from dusts at home, but depends more upon the change from poor management and the lack of firm control.

Asthmatic bronchitis is a disease common in children and young adults. Figure 3 shows the number of cases arranged according to decades of onset. In small children it is common, but a similar condition occurs in other ages. Skin tests are positive in a few cases, especially in the younger group. Nasal polyps are not common, presumably because the process is intermittent and is not associated with persistent advancing disease.

The term *asthmatic bronchitis* should be restricted to those cases in which isolated attacks occur at long intervals, mostly in winter. The asthmatic part is the allergy which can be demonstrated in numerous cases. When, for example, the family cat is removed, the colds are no longer wheezy. The bronchitis part is the new infection which starts the attack and lowers the threshold to make a slight allergy effective. If colds can be prevented, and the general health improved, the attacks do not occur. In other words, treatment can be directed either to the allergy or to the infection, and best, of course, to both factors at the same time.

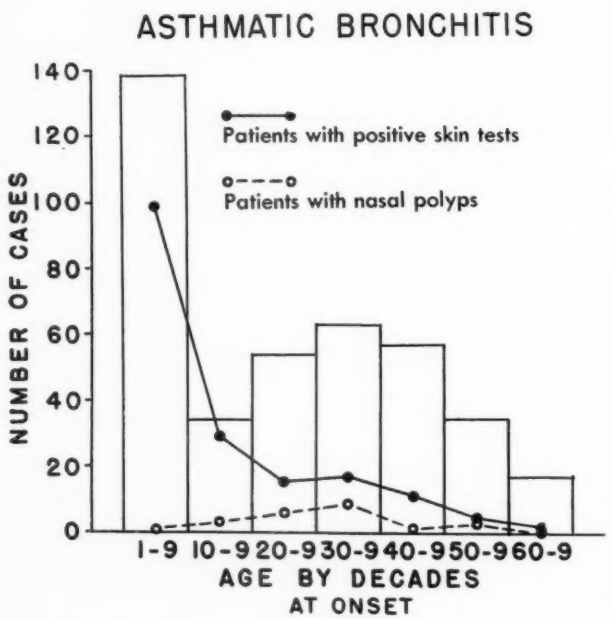


Figure 3

The *tired business man* and the *harassed housewife* are much alike. Both are apprehensive and suggestible, and in both the asthma may be severe. Organic and somatic factors may be present and treatment has been successful by such diverse methods as the extraction of bad teeth, radical operation on the sinuses, general rehabilitation, or merely by encouragement with vaccines and other active therapy. When these patients begin to gain weight, the asthma improves.

Emphysema may be primary or secondary. Primary emphysema is a serious disease in older men. It begins suddenly and the symptoms persist. Dyspnea and wheeze depend on exertion, and at rest the patient may be quite comfortable. The diagnosis is easy if an expression is remembered: "Emphysema sleeps well whereas asthma has bad nights." Treatment is difficult and the prognosis is not good, for this is a disease of the lungs, sometimes of the thoracic cage as well, and the symptoms depend upon a true pulmonary insufficiency. Secondary emphysema occurs in all asthma. It is a reversible process which comes and goes with each attack. The treatment here is of the basic cause.

Potassium iodide is the most useful drug. It loosens bronchial secretions, helps to prevent the formation of the tough, sticky plugs which can occlude the bronchial lumen. Diets, vaccines, treatment of the nose and sinuses, inhalation of aerosols of penicillin or other antibiotics must be considered, for one or the other may be indicated.

TREATMENT OF ASTHMA

The treatment of asthma has two parts—relief of the acute attack, and basic treatment.

For the acute attack general care is important. Many patients are frightened by their asthma. Confidence must be restored. Each must learn how to control his asthma and not let the asthma control him. Drugs are essential, especially the adrenergic drugs like epinephrine and ephedrine. Aminophylline is useful. Its action is quite different from that of epinephrine, but the mechanism is not yet quite clear. Morphine must never be used. It causes bronchospasm. Morphine has killed a number of patients. Chloral hydrate, paraldehyde, and ether are much safer. Fluids by vein, injected in large quantities, may be lifesaving. In each case "cure" and "care" go together.

Basic treatment consists of general measures. The physical examination, to look for other factors and other diseases, is essential and, again, encouragement and care of the patient as a whole are all important.

PROGNOSIS

In general, prognosis is good, for about 20 per cent of all patients with Intrinsic Asthma have been "cured" and another 60 per cent have been "improved."

Figure 4 shows the end results in cases of intrinsic asthma, again arranged according to decades at onset. Note that "cures" (in quotes) do occur and that improvement is frequent in each of the age groups. Death from other causes is likewise common and deaths from asthma occur with considerable frequency, and evidently more often in those who began their symptoms before age 50. Details of the follow-up studies are interesting.

Figure 5 (next page) is essentially a work sheet, for it shows the method of study and follow-up. Here are 50 cases in which asthma began at age 30—and after. They are arranged in chronological order according to the age at onset. Thus, five patients began at age 30, three at age 31, four at age 32, etc. Most of them are women; M indicates male patient.

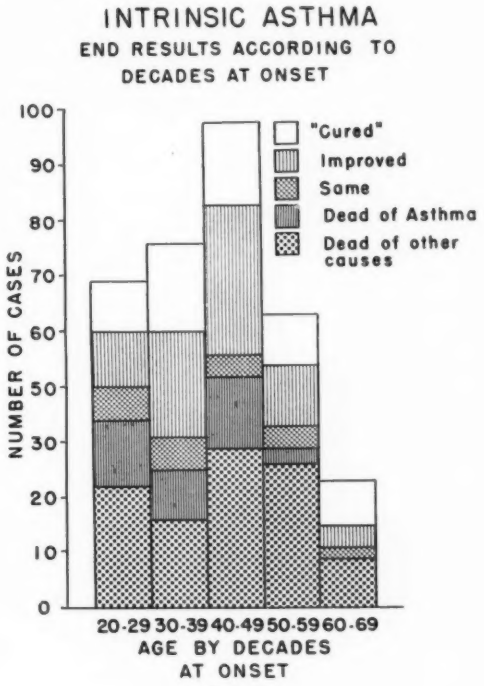


Figure 4

Each line is a case. It begins at the age when asthma began. The X marks the time of first observation and the character of the line, whether continuous for persistent asthma, or in dashes for attacks, or in dots for relief, indicates the progress. S stands for sinus operation. B means asthma better, and C means asthma "cured"—C1—indicating a further follow-up—still "cured." The black heart is a coronary death; the open heart means cor pulmonale; the black triangle means death from other causes; the black square is pneumonia; and the large black A means death from asthma itself, as proved at autopsy showing the lungs blown up and the bronchi filled with tough, sticky plugs.

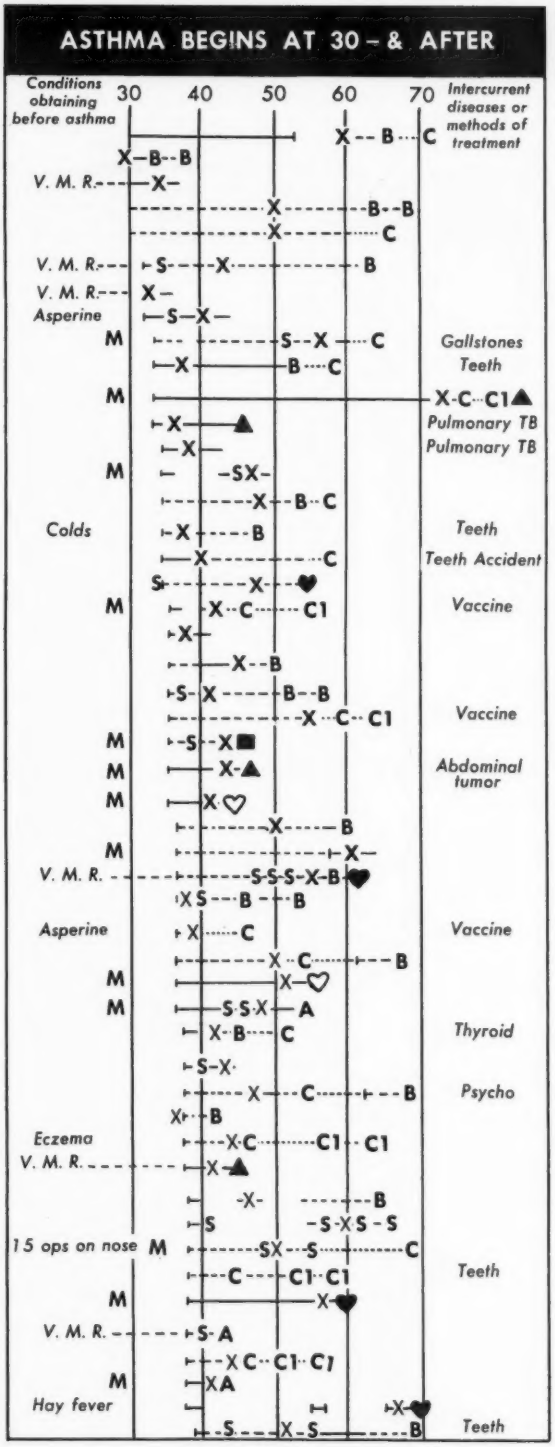


Figure 5

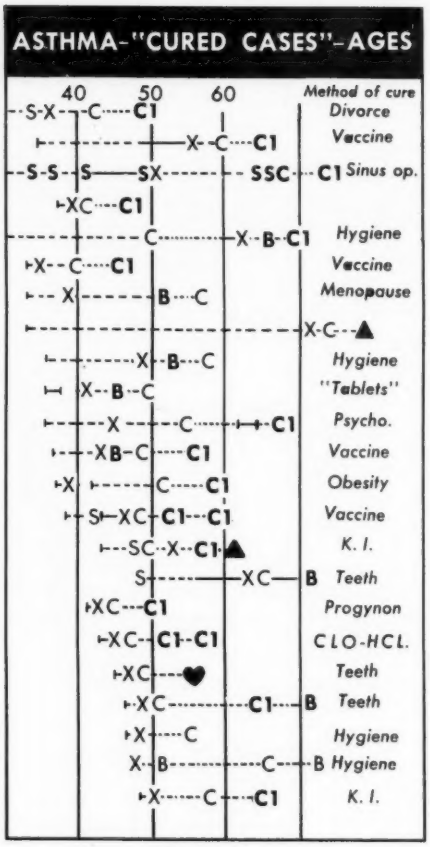


Figure 6

KEY

M	Male patient
A	Death from asthma
X	Time of first observation
——	Persistent asthma
– – –	Attacks of asthma
·····	Asthma relieved
S	Sinus operation
B	Asthma better
C	Asthma cured
C1	Further followup still cured
♥	Coronary death
♡	Cor pulmonale
▲	Death from other causes
■	Pneumonia

The words written to the left and the right in some of the cases indicate, on the left, conditions obtaining before the asthma or, on the right, certain intercurrent diseases, or certain methods of treatment after the asthma began: the removal of bad teeth, or the use of vaccines; tuberculosis and hyperthyroidism.

Figure 6 (page 138) shows a random sample of 23 cases taken from a larger number, all of whom have been relieved (c) of their asthma. Most of them are women. M indicates male patient. Note that in three cases the disease relapsed. At the last follow-up they were "B" (better) and no longer "C" ("cured").

The important part of the chart is the last column on the right, with words to summarize the method of cure as determined by the patient or his doctor. The list shows relief by such diverse therapy as vaccines, reducing diet, potassium iodide, removal of bad teeth, end of the menopause and, finally, by improved hygiene, which means the care of the patient as a whole—including the arrangement of divorce in one case! As noted, these methods have nothing to do with those of allergy. Dusts and foods were not changed; the patient was still living in the same environment; he was not "desensitized" to anything; his "cure" was not concerned with extrinsic factors.

PRESENT CONCEPTS

The diagram in Figure 7 (below) indicates that allergy is only one of four mechanisms by which the common denominator called "H Substance" is released and then causes a variety of symptoms. The diagram is helpful, if only because it raises a variety of questions such as those listed. The fact that from clinical evidence—from the end result of treatment—the answer is usually "Yes," requires that these questions must be considered seriously; the mechanism must be investigated.

Below the line on the diagram rheumatoid arthritis, peptic ulcer, colitis and migraine are noted, suggesting that a somewhat comparable diagram might be developed for them. Selye's important concept of his Adaptation Syndrome is very pertinent to this study, for he supports the idea that stress and strain can cause many symptoms, including asthma.

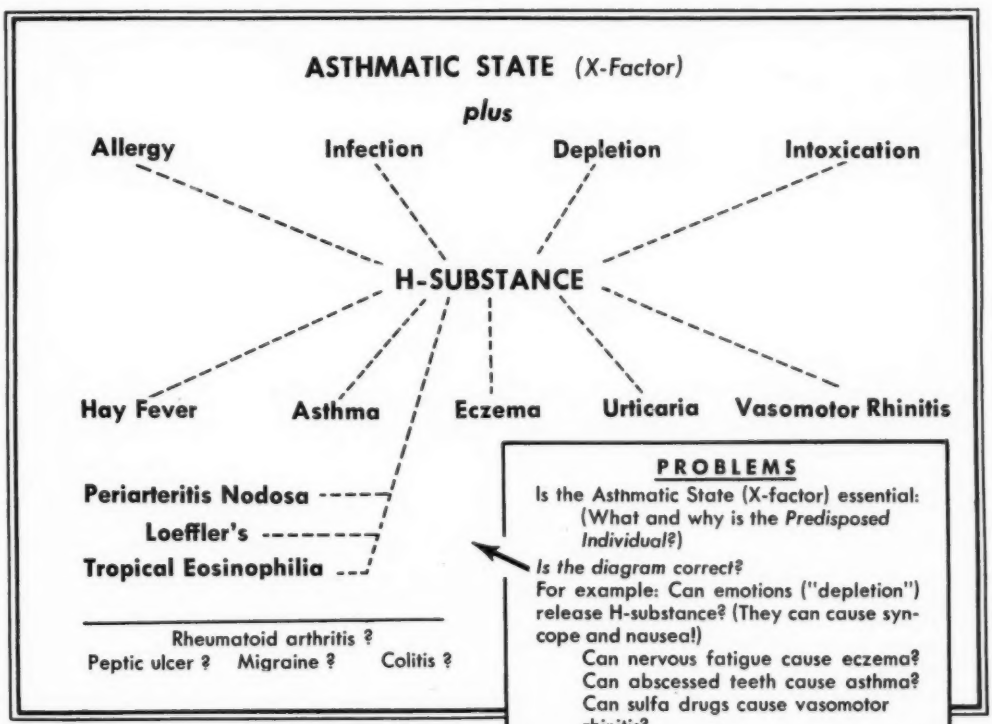
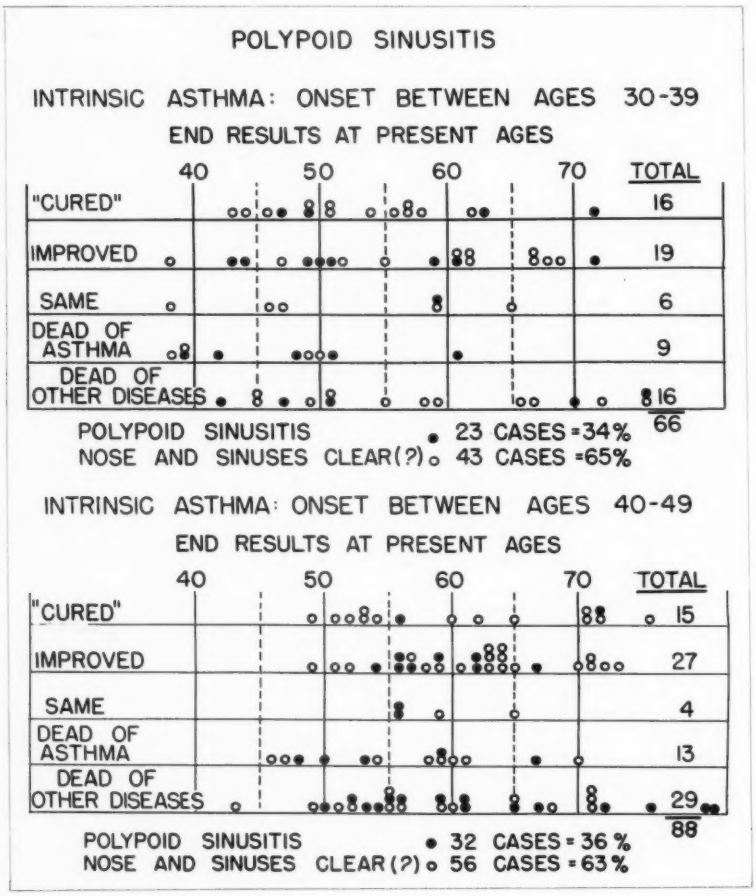


Figure 7

CERTAIN FACTS . . .	AND	. . . THEORIES
1. Predisposition to asthma Allergic disease in the family—often And in patient's own past history—sometimes		1. Bacterial allergy—from focal infection?
2. "All is not allergy that wheezes" Changes in season, residence or diet make no difference (even though tests may be positive)		2. Nerve reflex from nasal sinusitis? (Nasal lesion is part of the process, not a cause of it)
3. The heart remains "good" to the end		3. Deficiency of dietary intake—no evidence so far
4. The method of cure varies widely		4. Endocrine dysfunction? Will new studies in adrenal corticoids help us?
		5. Degenerative process? What is primary idiopathic structural emphysema? What lesions of pulmonary blood vessels?



The prognosis as related to the presence or absence of nasal polypoid sinusitis is illustrated above. The upper chart shows cases with onset between age 30 and 39; the lower, those between age 40 and 49. Sinus disease occurred in about one-third of all the cases, and the end results in that third are not quite so good as in the larger group whose sinuses were clear, but the differences are not too striking; the distribution of the black dots is fairly uniform throughout both charts.

EDITORIALS

Postgraduate Medicine OFFICIAL JOURNAL OF THE INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA — ORGANIZED IN 1915

Editor-in-chief: CHARLES W. MAYO, M.D.
Contributing Editor and Editorial Writer: MORRIS FISHBEIN, M.D.
Assistant Editor: SYLVIA COVET

AUGUST 1950

WORLD TRENDS IN POSTGRADUATE MEDICAL TRAINING

A RECENT survey among the national medical societies of the forty member countries of The World Medical Association reveals that, for postgraduate study and specialist training, the United States is more widely preferred by foreign physicians than any other nation polled.

Results of this world-wide study which we were able to complete only a short time ago show that of the 32 national groups responding to the questions, 23 included the United States in their respective lists of preferences. Great Britain scored second by being mentioned 18 times.

Specially designed to ascertain the current world trends in postgraduate medical education and specialist training, the study dealt largely with prevailing standards for specialists; period and type of training; prerequisites; examinations; certificates; schools; faculties; recognized specialties, and opportunities offered general practitioners for advanced education.

The investigation was one of several major projects which, already consummated or still in progress, have been undertaken by the Association to raise the standards of medical practice throughout the civilized world, consolidate professional cooperation on a global basis and thus contribute to international peace.

Among the more noteworthy facts disclosed in the survey were these:

1. Unlike the United States, 15 countries, ranging from Iceland to South Africa, require their physicians to meet certain *specific* standards before they can qualify as specialists. In three of these countries, Denmark, Greece, and Iceland, these standards are fixed exclusively by the government.

2. While the average minimum for the training of specialists in most countries is from two to three years, that of Cuba is only two months.

3. In 15 countries, including the United States, both theory and practice are required for specialization but Ecuador, Guatemala, Israel, Pakistan, and Peru have no postgraduate courses or schools.

Luxembourg has no medical faculties; therefore, their postgraduate work is done in other countries.

4. The United States, Norway, and Portugal are alike in that the supervision of graduate medical training is in the hands of the hospital staff. This responsibility varies rather widely in all other countries, Greece, for instance, entrusting it to a "committee of the Ministry of Health, President of the medical association and two professors . . ."

5. Only six countries—Denmark, Norway, Portugal, South Africa, Finland, and Greece—officially require general practice as a preliminary for specialization. In the United States, however, the specialist's training cannot be be-

gun before a hospital internship of one year.

6. The regular medical schools of 17 countries, including the United States, provide courses for specialist training and postgraduate education. In addition, this country, Great Britain, New Zealand, and Spain maintain institutions entirely restricted to such purpose.

7. In the United States, Great Britain, France, and nine other countries specialist qualifications acquired outside their respective boundaries are not recognized. (This, it is obvious, has particular bearing on those specializing physicians who, as displaced persons, seek to relocate in countries other than their own.)

8. The official medical society of India, with those of four other nations, admitted that local facilities for the postgraduate education of the general practitioner were insufficient. Yet India, alone, reported that even such limited facilities are infrequently used.

9. "The French Medical Association foresees a change from voluntary to compulsory education for various stages of professional life after graduation."

10. Teachers of postgraduate students in Iceland are not permitted to engage in private practice and those of New Zealand do not engage in research.

11. In contrast to the United States and twelve other countries, Great Britain is one of several nations suffering a scarcity of trained specialists.

The 32 national medical associations who cooperated in this survey represented the following countries:

> South Africa, Australia, Austria, Belgium, Canada, China, Cuba, Denmark, Dominican Republic, Eire, Ecuador, Finland, France, Great Britain, Greece, Guatemala, Iceland, India, Italy, Israel, Luxembourg, Netherlands, New Zealand, Norway, Pakistan, Peru, Philippines, Portugal, Spain, Sweden, Switzerland, and the United States.

In summing up the findings of this investigation we might say that, while confirming the medical profession of the United States in a position of world leadership, the facts are still sufficiently disturbing to make the unifying work of The Association even more imperative than it was before. Medicine, like art, recognizes no frontiers. As medical leaders, therefore, our first job is to keep the channels clear for the free, prompt, international exchange of scientific data. This, despite progressive diplomatic difficulties, is one of the objectives of The Association. By organizing eventually the 500,000 physicians represented in The World Medical Association behind uniformly high professional standards; by welding them into one solid confraternity, we are convinced that the health of all humankind will improve. Underlying such a goal are profound implications. Health, I think all of us will agree, is the necessary forerunner of any firm national economy. And again we will agree, I think, that a firm national economy must first be built before there can be an enduring world peace.

LOUIS H. BAUER, M.D.
Secretary-General
The World Medical Association

CHANGES IN BRITISH MEDICAL PRACTICE

THE whole tendency of medical practice in Great Britain under the National Health Act is to reduce the importance and responsibility of the general practitioner, practically eliminating him from the care of his patients in hospitals, and to exalt the specialist by giving him full control of patients who leave their general practitioner for hospital care. The status of the general practitioner has been under constant discussion since the act became effective. Recently a special committee of the British Medical Association, under Sir Henry Cohen, has developed a new report entitled "General Practice and the Training of the General Practitioner" which has aroused great interest and much discussion in Great Britain. Following are the functions and responsibilities of general practitioners as outlined by the committee:

1. Continuous Care of Patients—The general practitioner is the patient's own doctor or family doctor.
2. Health Education and Preventive Medicine—No one else is in so advantageous a position to give advice. He knows the circumstances and job of his patient, his family problems and responsibilities.
3. Treatment of the Patient as an Individ-

ual—He must have regard to the totality of his patient, his distinctive personality, home environment, occupation, emotional make-up, medical history.

4. Diagnosis—The trivial illness, the serious, the fanciful, the real follow one another in quick succession, and it is the responsibility of the practitioner to sort them out and to decide quickly and firmly the course to take.
5. Treatment—Includes prescribing and dispensing, various technical procedures, minor surgery, psychologic help, and preventive measures.
6. Emergency Treatment—Skill in first aid.
7. Information to Specialists—The general practitioner is looked to for the fullest possible information about the patient who is sent for opinion or treatment.
8. Aftercare and Rehabilitation—The patient generally needs not only convalescence and aftercare but careful supervision even after return to work.
9. Administrative and Legal Requirements—Statutory certifications, liability to give evidence in court, compliance with administrative regulations under the N.H.W.
10. Miscellaneous Work—Part-time appointments in the public health service or industrial concerns, schools, or medical institutions.
11. Nonmedical Duties—Involving personal qualities which defy analysis. Answering such questions as "Should Sally marry a boy who is earning 15 a week?" or "Should I make it up with my sister?"

A careful analysis of these eleven responsibilities indicates that after all in Great Britain at least, the general practitioner is coming to be an inferior medical citizen. Notwithstanding this allocation of responsibilities to the general practitioner and the recognition that the general practitioner is likely to refer all cases to specialists, the committee recites the personal qualities that are desired in a general practitioner, admitting that anybody that met these qualifications could easily be called "superman." Thus the general practitioner should have "tact, wisdom, patience, discretion, imperturbability (Osler's word), gentleness, firmness, ability to inspire confidence and trust, kindness and humanity, being all things to all men, guide, philosopher, and friend to patients of all classes, equally at ease with duke and dustman, and, along with all this, a sound medical knowledge, the ability to do patient, practical work and to apply scientific methods, observation, discrimination, selection, diagnosis, and decision."

With all this, the general practitioner will of course put in innumerable hours at hard work, sacrifice most of his home life, develop good health and stamina in order to last at least a few years, and pick out a wife who is willing to share the burden and sacrifice. For all this he gets a fairly good standing in his community and a knowledge that he is helping people.

Incidentally the committee points out that the general practitioner should be a man of culture with a hobby or outside interest. He should participate in the social life of his neighborhood—but the committee does not say when or how. The committee recognizes that modern advances in medicine have made the keen general practitioner far more able than was the general practitioner of the past to treat at home patients who formerly would have been sent to hospitals. The management of pneumonia is the most conspicuous example.

The committee does deplore the divorce of the general practitioner from the hospital. Listed as ways in which a general practitioner could work in the hospital are the following five allocations:

1. Midwifery.
2. Routine care of cases admitted either as medical emergencies or for operation by one of the visiting consultants.
3. Assisting at operations on these cases.
4. Consultations with visiting specialist staff.
5. Minor surgery and accident emergencies, for which a weekly rota of the local doctors is provided.

Apparently the activities of the World Medical Association have had some influence because the committee supports from an educational standpoint the increasing demand for hospitals and wards in hospitals in which the general practitioner may serve. When his patient is in the hospital, the general practitioner should be permitted at all reasonable times to visit him; the hospital

staff should keep the general practitioner in touch with the patient's progress. The committee recognizes finally that there must be more doctors in England, that each doctor should have a smaller number of patients in his care and that readjustments in remuneration must be made to provide proper income with a lesser number of patients. Thus will the standard and status of general practice be raised.

Certainly the British committee is to be commended on the quality and understanding of its report. One expects idealism in these reports but the editor of the *British Medical Journal,* commenting on the report, has this to say: "After nearly two years of the National Health Service it has become increasingly clear that general practice has suffered and hospitals have benefited, at least financially, from the new regime. None can deny that the public will best be served by having a strong general-practitioner service, backed up by well-equipped hospitals. The present disparity between the development of general practice and hospitals is ultimately to the detriment of both. General practitioners have lost work which should be done by them, and hospitals have been burdened beyond their capacity."

Moreover the editor of the *British Medical Journal* reminds the committee that health centers which would provide general practitioners not only with opportunities for meeting their professional colleagues but also with the leisure to maintain themselves as cultured and informed members of the community were promised as a significant portion of the National Health Service but have thus far failed to appear. In the lack of such health centers, the hospitals should attempt to meet the needs of general practitioners for laboratory service. The well trained general practitioner should have the right to maintain laboratory investigation of his own patients. Thus he will be better able to determine promptly when specialist services are needed.

MORRIS FISHBEIN

INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA

OFFICERS OF THE ASSOCIATION

PRESIDENT
Dr. Waltman Walters, Rochester, Minn.

PRESIDENT-ELECT
Dr. Richard B. Cattell, Boston, Mass.

PRESIDENTS OF CLINICS
Dr. John F. Erdmann, New York, N. Y.
Dr. Frank H Lahey, Boston, Mass.

MANAGING DIRECTOR
Dr. Arthur G. Sullivan, Madison, Wis.

SECRETARY
Dr. Tom B. Throckmorton, Des Moines, Ia.

TREASURER AND DIRECTOR OF FOUNDATION FUND
Dr. Henry G. Langworthy, Dubuque, Ia.

SPEAKER OF THE ASSEMBLY
Dr. Mather Pfeiffenberger, Alton, Ill.

BOARD OF TRUSTEES
Dr. Edwin S. Hamilton, Kankakee, Ill.
Dr. Mather Pfeiffenberger, Alton, Ill.
Dr. Maurice R. Williamson, Alton, Ill.
Dr. Henry G. Langworthy, Dubuque, Ia.
Dr. John E. O'Keefe, Waterloo, Ia.
Dr. Tom B. Throckmorton, Des Moines, Ia.
Dr. John M. Dodd, Ashland, Wis.
Dr. Eugene S. Sullivan, Madison, Wis.
Dr. Stephen E. Williams, Chippewa Falls, Wis.

EDITOR-IN-CHIEF, POSTGRADUATE MEDICINE
Dr. Charles W. Mayo, Rochester, Minn.

COMMITTEE ON MEDICAL RESEARCH AND ADVANCEMENT
Dr. Elliott P. Joslin, Boston, Mass.
Dr. W. Wayne Babcock, Philadelphia, Pa.
Dr. Charles H. Best, Toronto, Ont.
Dr. George Crile, Jr., Cleveland, Ohio
Dr. Evarts A. Graham, St. Louis, Mo.
Dr. Roy D. McClure, Detroit, Mich.
Dr. Jonathan C. Meakins, Montreal, Quebec
Dr. Eric Oldberg, Chicago, Ill.
Dr. James E. Paullin, Atlanta, Ga.
Dr. Erwin Schmidt, Madison, Wis.
Dr. Waltman Walters, Rochester, Minn.

PROGRAM COMMITTEE
Dr. Russell L. Cecil, New York, N. Y.
Dr. Henry A. Christian, Boston, Mass.
Dr. John R. Fraser, Montreal, Quebec
Dr. Duncan A. L. Graham, Toronto, Ont.
Dr. Herman L. Kretschmer, Chicago, Ill.
Dr. Frank H. Lahey, Boston, Mass.
Dr. Charles F. Martin, Montreal, Quebec
Dr. Charles W. Mayo, Rochester, Minn.
Dr. Howard C. Naffziger, San Francisco, Calif.
Dr. Charles H. Phifer, Chicago, Ill.
Dr. Leonard G. Rowntree, Miami, Fla.

HONORING THE ONE HUNDREDTH ANNIVERSARY
of the founding of the

GEORGETOWN UNIVERSITY SCHOOL OF MEDICINE

POSTGRADUATE MEDICINE

ANNOUNCES FOR SEPTEMBER

a special issue featuring articles on advances in Medicine and Surgery by members of the faculty of the Georgetown Medical Center

Progress in Anesthesiology—
EDWARD B. TUOHY

Common Problems in Coronary Artery Disease—
STEPHEN N. JONES AND THOMAS F. KELIHER

Diagnosis and Treatment of Acute Pancreatic Disease—
ROBERT J. COFFEY, EARL B. BARNES, PAUL REED AND FREDERICK B. BRANDT

Carcinoma of the Upper Rectum and Rectosigmoid—
GARNET W. AULT, A. F. CASTRO AND ROBERT S. SMITH

Bacteriologic Studies in the Diagnosis of Infectious Diseases—
SAMUEL SASLAW

The Hypersensitive Carotid Sinus—
J. ROSS VEAL AND RICHARD BAUERSFELD

Meckel's Diverticulum as the Source of Massive Intestinal Hemorrhage—FRED R. SANDERSON AND FRANCIS A. BARRETT, JR.

Splenectomy in Leukemia—
OSCAR B. HUNTER, JR. AND PAUL C. KIERNAN

Polyps of the Large Bowel—
C. EDWIN MCNAMARA

Hemophilia Simulating Acute Surgical Abdomen—
MARGARET M. K. SHELTON AND HUGH H. HUSSEY

Some Problems Presented by Cranial Defects—
O. HUGH FULCHER AND ARTHUR A. MORRIS

The Modern Treatment of Rheumatoid Arthritis—
DARRELL C. CRAIN, LAURENCE H. KYLE AND MARTIN RUBIN

Pulmonary Function Studies in Surgery—
JOHN J. CURRY AND FRANK ASHBURN

in addition to POSTGRADUATE MEDICINE'S *special features and regular monthly departments*

The Medical Bookman

OFFICE ORTHOPEDICS*

I AM impressed by this book as a contribution to the work of the general practitioner. An unusual arrangement puts a general bibliography first and follows it with a chapter on the materials used in the practice of orthopedics. Here is all the armamentarium necessary for applying plaster casts and splints of many types. A special bibliography in this portion fails to mention a booklet circulated without cost by Johnson & Johnson to anyone who wants it which tells more about application of the material of orthopedics than any other work I know and tells it too with many illustrations that make learning simple.

Next to the paraphernalia for application to the patient are the methods and materials of physical therapy. The presentation is brief and enlightening. Another preliminary chapter is concerned with local anesthesia.

The general practitioner will find Section II, which takes up each of the special sections of the body of concern in orthopedics, brief, practical and intensely informative. The sections headed ingrown toenails, corns and callouses, metatarsal pain, and shoes are an indication of the character of the useful material. Similarly the ankle and the calf, the knee, and particularly the back are given explicit and didactic consideration.

Part III should be especially commended because of its approach to practice of orthopedics by general practitioners. Limp, crooked back, flatfoot, clumsiness and painful arms or legs in the child and adult are subjects given special consideration. The inability of a child to sit up, weakness, interpretation of roentgenograms are additional sections. Each chapter is supplemented by a bibliography which gives reference to easily available material.

One hundred and fifty-six illustrations scattered liberally throughout the text are definitely an aid to the instruction.

The index is as adequate as the rest of the book.

M. F.

*Office Orthopedics. By Lewis Cozen, M.D., F.A.C.S., Attending Orthopedic Staff: The Orthopedic Hospital, Veterans Hospital, Los Angeles County Hospital, Cedars of Lebanon Hospital, and Los Angeles Tuberculosis Sanitarium, Monrovia, California; Assistant Professor of Orthopedic Surgery, College of Medical Evangelists, Los Angeles. 232 pages with 156 illustrations. Philadelphia, Lea & Febiger, 1950. $5.00.

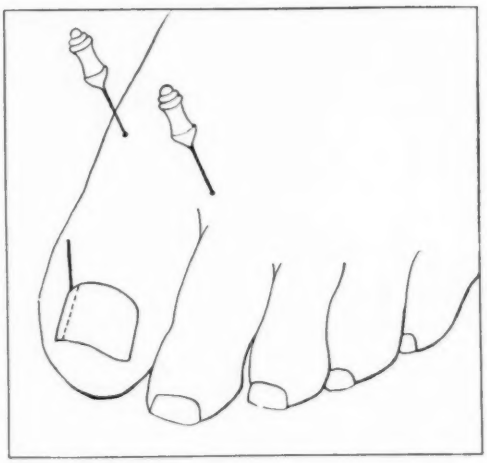


FIGURE 25A. Office operation for ingrown toenail. The portion of the nail to be removed is indicated by the dotted line. The line of excision is continued downward to include the segment of nail under the skin and the matrix of that portion of the nail is curetted.

FIGURE 146. Figure eight plaster bandage for fractures of the clavicle. *(Illustrations from: "Office Orthopedics.")*

► 1949 YEAR BOOK OF DRUG THERAPY - - -

Edited by Harry Beckman, M.D., Director, Department of Pharmacology, Marquette University School of Medicine. 718 pages, illustrated. 1950, The Year Book Publishers, Inc., Chicago, Illinois. $4.75.

The 1949 Year Book of Drug Therapy edited by Harry Beckman carries on the tradition for thoroughness and excellence established by its predecessors. The major headings in the table of contents suggest the great variety of information on virtually all the branches of medical practice available in this volume, which covers therapy in: Allergy, Cardiovascular Diseases, Dermatology, Endocrinology, Gastroenterology, Hematology, Internal Medicine, Neuropsychiatry, Obstetrics, Ophthalmology, Otorhinolaryngology, Pediatrics, Roentgenology, Surgical Specialties, and Venereal Diseases.

In what condition may Antabuse for alcoholism be contraindicated? What dosage is advisable in penicillin troches for rheumatic fever prophylaxis? What foreshadows abnormal cardiac rhythms due to digitalis? Why is there no satisfactory method of stimulating spermatogenesis? For the answers to these and hundreds of other pertinent pressing and practical questions you are referred to the current year book of drug therapy.

E. B. C.

► A MANUAL OF CARDIOLOGY - - -

By Thomas J. Dry, M A., M.B., Ch.B., M.S. in Medicine; Associate Professor of Medicine, University of Minnesota (Mayo Foundation); Consultant in Section on Cardiology, Mayo Clinic. New, 2nd Edition. 355 pages, with 97 figures. 1950, W. B. Saunders Company, Philadelphia & London. $5.00.

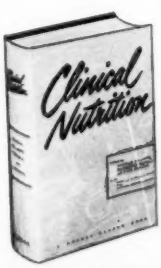
Dr. Dry has completely revised his first edition and again has comprehensively covered the diseases of the heart and circulation in a condensed and precise form. He has separated the "chaff and the grain" from the first book and with unusual gift of refinement has brought the field up to date to meet the advances that have taken place so rapidly.

This small volume meets the requirements of the medical student, the busy general practitioner, and the internist. It is easily readable, well arranged in orderly and logical sequence and is illustrated with x-rays and electrocardiograms. The chapters on Congenital Heart Disease, Electrocardiography, Congestive Failure Therapy and Subacute Bacterial Endocarditis reflect the important advances that have been made since the first edition. A new chapter deals with heart disease as it is related to pregnancy, anesthesia, and surgical operations.

R. W.

► CLINICAL NUTRITION - - -

Edited by Norman Jolliffe, Frederick F. Tisdall and Paul R. Cannon. 36 contributors. 925 pages, 127 illustrations including 61 color plates. 1950, New York, Paul B. Hoeber, Inc. $12.00.



This book is sponsored by the Food and Nutrition Board of the National Research Council, a circumstance which assures authenticity. The editors are accredited students of nutrition and among the collaborators are Best, Elman, Keys, Moore, Newburgh, Snapper, Soskin, Spies, and Wilder. The text is divided into three parts. Part one is concerned with diagnosis, and elucidates physical phenomena, laboratory tests, and roentgenographic signs characteristic of the several deficiency diseases. The colored pictures of abnormal appearances of the skin and tongue included in this section are excellent, and chosen with discrimination. Interpretation of dietary histories as an aid to diagnosis is properly stressed.

Part two comprises biochemical and physiologic discussions of separate and particular deficiencies. Part three is devoted to therapy and prevention of nutritional deficiencies. Instructions are given for planning adequate diets for many specific diseases in the treatment of which derangement of normal balance of food and fluid elements is required. The appendix contains food tables and sample diets appropriate for all deficiencies.

The arrangement of the comprehensive material is adapted to information and instruction of students and to reference and refreshment by practitioners of medicine and nutrition. J. B. C.

► MEDICAL MANAGEMENT OF GASTROINTESTINAL DISORDERS - - -

By Garnett Cheney, M D., Clinical Professor of Medicine, Stanford University Medical School. 478 pages, illustrated. 1950, The Year Book Publishers, Inc., Chicago. $6.75.

In this text the field of medical management of gastrointestinal disorders is presented in a fashion quite apart from most textbooks. The first portion of the book is devoted to the patient approach which includes the examination of patients with routine and special procedures. In some respects this portion seems very elementary since considerable space is devoted to history taking, fundamentals of physical examination, and routine laboratory studies. This text is, however, excellent for students who are for the first time faced with the subject of clinical medicine and also to the general practitioner who wishes to have a concise outline for refreshing his memory for fundamentals and methods of treatment. Long, drawn-out dissertations and academic arguments are conspicuously omitted.

The second part of the book covers the symptom diagnosis and treatment, including indications for surgery. In this section, twenty-four major subdivisions are discussed under common complaints such as sore mouth and tongue, indigestion, weight loss, etc., as well as major categories such as gallbladder disease and liver disease.

For lengthy historical and theoretical considerations the reader should refer to other sources, but for realistic and practical aspects of the management of gastrointestinal diseases, the physician will welcome this text to his library.

Y. S.

► MEDICAL GYNECOLOGY - - -

By James C. Janney, M.D., F.A.C.S., Associate Professor of Gynecology, Boston University School of Medicine; Associate Visiting Gynecologist, Massachusetts Memorial Hospital. New, 2nd Edition. 454 pages, with 108 figures. 1950, W. B. Saunders Company, Philadelphia & London. $6.50.

In this text the author has attempted to correlate the clinical practice of office gynecology with didactic teaching by stressing the cause of symptoms, the correct interpretation of findings, and the physiologic basis for the therapy. This is accomplished by orderly arrangement of the text in logical sequence starting with a review of history taking and physical examination. Although repetition is didactically desirable and difficult to avoid in this type of text, some duplication such as in figures 73 and 82 could well be eliminated.

This edition retains the same general outline as the first, but includes discussions of newer developments such as antibiotics, antispasmodics, hormones, basal temperature records, Papanicolaou smears, and culdoscopy. Failure to omit some obsolete procedures from the text is notable. Examples of this include an illustration of apparatus for tubal insufflation employing the hand bulb and a brief chapter devoted to foreign protein therapy.

The author ascribes endocrine activity to dysgerminoma and cystadenoma which is contrary to general opinion. Despite these criticisms the text should be valuable to medical students and general practitioners as a practical guide in the correlation of clinical and didactic gynecology.

M. B. S.

► APPLIED MEDICINE - - -

By G. E. Beaumont, M.A., D.M., F.R.C.P., D.P.H., Physician to the Middlesex Hospital and Hospital for Diseases of the Chest, Brompton. 540 pages, with 74 illustrations. 1950, The Blakiston Company, Philadelphia & Toronto. $6.00.

Dr. Beaumont has drawn from his twenty-five years of private and hospital practice to present some problems in diagnosis and treatment that have first come to the notice of the general practitioner and have then been referred to the consultant. Recognizing that the complete textbook case is rarely encountered (since the textbooks of necessity present a composite picture of all the possible variables), Dr. Beaumont feels the need for individual description of disease. He therefore presents detailed descriptions of individual cases, emphasizing the symptoms experienced by the pa-

tient, the patient's reaction to the disease as well as the detailed observation of the physician.

The appeal and value of this book lie in the appeal and value of clinical ward teaching. The first three parts of this book deal with Descriptive Cases, Short Notes on Cases, and Cases demonstrated at bedside by question and answer. In every case of this treatise, the patient is presented to the reader in such a manner as to enable one to develop his own diagnosis and method of investigation. Upon conclusion of the case there are pertinent discussion, comment and reference. The chapters are filled with illustrations, diagrams, x-rays, and charts whenever needed to emphasize the clinical picture at hand.

This book is recommended highly to all who enjoy classical reading and who enjoy the challenge and stimulus of diagnostic problems.

R. W.

Books received will be acknowledged in this department each month. As space permits, books of principal interest to our readers will be reviewed more extensively.

Office Treatment of the Nose, Throat and Ear. By Abraham R. Hollender, M.Sc., M.D., F.A.C.S., Professor of Otolaryngology, Emeritus, University of Illinois College of Medicine; Attending Otolaryngologist, St. Francis Hospital and Mt. Sinai Hospital, Miami Beach; Consulting Otolaryngologist, Variety Children's Hospital, Miami, Florida. Ed. 3. 620 pages, illustrated. 1950, The Year Book Publishers, Inc., Chicago. $7.50.

The Cerebral Cortex of Man. By Wilder Penfield, C.M.G., M.D. (Johns Hopkins), B.Sc. and D.Sc. (Oxon.), Hon. F.R.C.S. (Lond.), F.R.S., Professor of Neurology and Neurosurgery, McGill University; Director, Montreal Neurological Institute; and Theodore Rasmussen, M.D., Professor of Neurological Surgery, The University of Chicago. 248 pages, with 121 figures. 1950, The Macmillan Company, New York. $6.50.

A Short Textbook of Radiotherapy. By J. Walter, M.A., B.M., M.R.C.P., D.M.R.E., Deputy Medical Director, Sheffield National Centre for Radiotherapy; and H. Miller, M.A., Ph.D., F. Inst. P., Physicist, Sheffield National Centre for Radiotherapy. 444 pages, with 199 illustrations. 1950, The Blakiston Company, Philadelphia & Toronto. $6.00.

Atlas of Human Anatomy. By M. W. Woerdeman, M.D., F.R.N.A.Sc., Professor of Anatomy and Embryology and Director of the Department of Anatomy, University of Amsterdam. Volumes I and II. Volume I: Osteology, Arthrology, and Myology. 512 plates. $10.00. Volume II: Splanchnology, Angeiology, Nervous System, and Organs of Sense. 642 plates. $10.00. 1950, The Blakiston Company, Philadelphia & Toronto. Volumes I and II—$18.00.

The Merck Manual of Diagnosis and Therapy. Ed. 8. 1592 pages. 1950, Merck & Co., Inc., Rahway, New Jersey. Regular edition, $4.50; thumb-index edition, $5.00.

Peptic Ulcer. By A. C. Ivy, Ph.D., M.D., D.Sc., LL.D., Vice President of the University of Illinois in Charge of Chicago Professional Colleges; M. I. Grossman, Ph.D., M.D., Associate Professor of Physiology, University of Illinois, College of Medicine; and William H. Bachrach, Ph.D., M.D., Research Associate in Physiology, University of Southern California, School of Medicine. 1,144 pages, with 137 illustrations and 210 tables. 1950, The Blakiston Company, Philadelphia & Toronto. $14.00.

Genealogy of Gynaecology. By James V. Ricci, M.D., Clinical Professor of Gynaecology and Obstetrics, New York Medical College; Attending Gynaecologist, City Hospital, New York; Consultant in Gynaecology and Obstetrics, Beekman-Downtown Hospital; Director of Gynaecology and Obstetrics, Columbus Hospital. Ed. 2. 494 pages. 1950, The Blakiston Company, Philadelphia & Toronto. $8.50.

Nutrition in Ophthalmology. By John J. Stern, M.D. 137 pages. 1950, The National Vitamin Foundation, Inc., New York. $1.50.

Recent Advances in Chemotherapy. By G. M. Findlay, C.B.E., Sc.D., M.D., F.R.C.P., Editor, Abstracts of World Medicine and Abstracts of World Surgery, Gynaecology and Obstetrics, British Medical Association, London. Ed. 3, Vol. 1. 625 pages. 1950, The Blakiston Company, Philadelphia & Toronto. $7.50.

Nutrition and Diet Therapy. By Fairfax T. Proudfit, Formerly Instructor in Nutrition and Diet Therapy, University of Tennessee College of Medicine and University of Tennessee School of Nursing; Director of Dietary Department, John Gaston Hospital, Memphis, and Corinne Hogden Robinson, Lecturer in Nutrition and Dietetics, Temple University School of Medicine, Philadelphia. Ed. 10. 950 pages, illustrated. 1950, The Macmillan Company, New York. $4.00.

Modern Practice in Dermatology. Edited by G. B. Mitchell-Heggs, O.B.E., M.D., F.R.C.P., Physician-in-Charge, Skin Department, St. Mary's Hospital and Medical School, London; Physician, St. John's Hospital for Diseases of the Skin and Institute of Dermatology, University of London. 836 pages, with 319 figures, and 7 color plates. 1950, Paul B. Hoeber, Inc., New York. $12.50.

Saints, Sinners and Psychiatry. By Camilla M. Anderson, M.D., Assistant Professor of Psychiatry, University of Utah. 206 pages. 1950, J. B. Lippincott Company, Philadelphia, London & Montreal. $2.95.

Currents in Nutrition; Proceedings of the Nutrition Symposium, The University of Illinois, College of Medicine, November 19, 1949. By Bertha Burke, William J. Darby, L. Emmett Holt, Jr., M. K. Horwitt, Ancel Keys, Carl V. Moore, James M. Strang and R. W. Vilter. 128 pages. 1950, The National Vitamin Foundation, Inc., New York. $1.00.

World Surgery 1950. By Stephen A. Zieman, M.A., M.D., F.A.C.S., F.I.C.S., Abstract and News Editor, Journal of the International College of Surgeons, Abstractor for International Abstracts of Surgery and Surgery, Gynecology & Obstetrics. 1-7 pages, with 53 illustrations. 1950, J. B. Lippincott Company, Philadelphia, London & Montreal. $6.00.

Manual of Rheumatic Diseases. By W. Paul Holbrook, M.D., and Donald F. Hill, M.D., Tucson, Arizona. With the assistance of Charles A. L. Stephens, Jr., M.D. 182 pages, with 119 figures. 1950, The Year Book Publishers, Inc., Chicago. $4.25.

Human Sterilization; Techniques of Permanent Conception Control. By Robert Latou Dickinson, M.D., and Clarence James Gamble, M.D. 40 pages, illustrated. 1950, Waverly Press, Inc. Available upon request to Dr. Dickinson, 501 Madison Ave., New York 22, N. Y.

Plan Now

to Attend the 35th Annual International Assembly

of the Interstate Postgraduate Medical Association

to be held in

Chicago, November 6

through November 9, 1950

• An outstanding opportunity to bring yourself abreast of the latest developments in medicine, including methods, diagnosis and treatment.

Directed to the practice of general medicine, 56 medical experts from the United States, Canada, and England will present the latest dependable, technical, medical information.

31 Diagnostic Clinics
25 Lectures

A total of 56 top quality, up to the minute, fact packed half hour presentations by national and international leaders.

A 4-day postgraduate course, conducted on an exact time schedule, where the specialties are translated into general practice, and the specialists attend to broaden their clinical horizons.

MARK These Important Dates on Your Calendar NOW!

A large number of patients are demonstrated daily

Consultation Service

This special consultation information service is offered as a regular monthly feature of *Postgraduate Medicine*. Subscribers are invited to call on this Service for answers to difficult medical problems from members of our Editorial Board and our Editorial Consultants best qualified to help. Each question will be answered by mail and those of general interest will be published each month. Address all communications to Consultation Service, *Postgraduate Medicine*, 516 Essex Building, Minneapolis 3, Minnesota.

PHYSICIAN SEEKS HELP FOR SYMPTOMS OF PARKINSON'S DISEASE

QUESTION: Will you please publish this letter in the hope that I get some measure of relief from your readers who may come across this letter.

I am suffering with postencephalitic parkinsonism, and I am being plagued by a series of symptoms which I will try to describe, starting from the minor symptoms, and going on to the more serious.

The first symptom is rigidity of the muscles, and I find it most difficult to get out of a chair from the sitting position, and it is also very hard for me to hold up my head, and I stoop forward very much with my head down all the time.

My second symptom is the tremor of my left arm and hand which is markedly exaggerated when I try to chew and when I try to swallow which I cannot do. Tremor bothers me very much. It started with the left thumb, and has invaded my left hand and arm.

My third symptom is the inability to swallow which is the most serious of all. I just cannot swallow, and this exaggerates my tremor. I fear eating very much because I cannot swallow.

And the next symptom is just as annoying as the latter, and it is that of hypersalivation. This is very annoying, and it is so bad that I cannot carry on a running conversation. The saliva keeps pouring out as from a spigot, and I am constantly drooling, and I just cannot swallow, so you can see how embarrassing it is for me. I surely would want to get some relief for that condition. Of these last two symptoms I would say that the inability to swallow is the worst, and the hypersalivation is the next serious.

I hope that the medical men will send me some good suggestions, and thereby give me some measure of relief.

DR. T. M.

Replies to this inquiry, addressed in care of POSTGRADUATE MEDICINE, will be forwarded to Dr. T. M.

SURGICAL PROCEDURE FOR VARICOSE VEINS

QUESTION: What do you consider good varicose vein surgical procedure for an occasional operator who has an intern to assist him? In a well organized hospital staffed with specialists and residents, a surgeon and his resident do a high ligation, then excise all the varicose veins in the legs as well as the perforators, front and back, the surgeon doing one leg, the resident the other, simultaneously—a procedure that takes them three to five hours. But what about the operator who doesn't have the advantage of the services of a well trained resident? For him to do both legs, front and back himself with the intern assisting, would take him all day. What should be the extent of his surgical procedure consistent with obtaining a good result?

M.D.—California

ANSWER: The type and extent of the surgical procedure required for the relief of varicose veins will vary from patient to patient. After levels of incompetency have been determined by appropriate tests, i.e., comparative tourniquet, Trendelenburg, Perthes, generally three courses are open to the surgeon: (1) performing indicated stripping, excision, etc., in one stage; (2) staging these procedures over a period of weeks, and (3) doing simple ligations at indicated levels of incompetency with the full realization that this therapy falls short of the ideal and recurrences are likely to occur.

MICHAEL E. DEBAKEY

TREATMENT OF MYOCARDIAL INFARCTION

QUESTION: In a patient who is fibrillating during a myocardial infarction seige—say the tenth day, she develops auricular fibrillation along with shock and increased left shoulder pain—can 10 cc. of 1 per cent procaine (100 mg.) be used for therapy? If digitalis should be given, when should the first dose be given and how much digitalis? Can anything be done in such a patient who is digitalized (0.5 mg. Digoxin every four hours) to prevent embolic phenomena?

Where do most of the clots come from which produce a pulmonary embolus? Legs? Pelvis? Right auricle? If the latter, could cardiac catheterization of the right auricle (with suction) be done prior to digitalization with the hope of ensnaring a dangling thrombus? It is assumed that dicumarol therapy has been and is being used.

Is there any contraindication to giving heparin to a diabetic who is fibrillating and in shock from a myocardial infarction? (BS 250 mg.).

M.D.—Windsor, Ontario

ANSWER: This question covers many highly controversial points in the treatment of diseases of the cardiovascular system. From the facts given, an extension of the original myocardial infarction is most likely.

Classical treatment, consisting of rest, reassurance, morphine, atropine, oxygen and re-evaluation of the anticoagulant schedule is preferred as procaine would attack only the pain. Digitalis whole leaf in a dosage of 3 gr. (0.2 gm.) three times daily should be used for frank congestive failure and to

slow ventricular rates much over 100 per minute in the presence of auricular fibrillation. Of course a low salt diet and mercurial diuretics could very easily diminish the edema.

The answer to the original source of emboli is not easy. Probably most emboli arise in the deep leg veins, the pelvic veins, the atria and auricular appendages and from the endocardial surface of large myocardial infarcts. Thrombus formation is much commoner in elderly people in debilitated states with complete bed rest. There is no proof that digitalis accelerates thrombus formation. For obvious technical reasons, venous catheterization is contraindicated for thrombus removal, not to mention the obvious danger of inducing further shock and ventricular fibrillation.

Finally there is no contraindication to the use of either heparin or dicumarol in such a patient, if a good laboratory is available. Clotting time should be determined before intermittent heparin usage. Prothrombin times should be obtained before dicumarol is administered and also obtained daily during administration. (For further details see the following reference: Stroud and Stroud: Recent developments in the management of congestive heart failure. M. Clin. North America, page 563, 1950.)

WILLIAM D. STROUD AND MORRIS W. STROUD, III

INTRAVENOUS PROCAINE FOR HEADACHES

QUESTION: I have a patient, white female, age 52, who has periodic headaches behind one or the other eyeball. They occur about every three weeks and last from one to three days. Nothing seems to alter the frequency or duration. She is in pain unless asleep and at present the best sedative seems to be seconal and sodium phenobarbital. She has been tried on the usual migraine treatments: dihydroergotamine, antihistamines, oxygen inhalation, histamine therapy (including intravenous drip).

Are there any reasons to think that intravenous procaine will help? Are there any contraindications? She has moderate arteriosclerosis and occasional angina pectoris.

I would like any information on intravenous procaine, indications, and dangers.

M.D.—South Carolina

ANSWER: A brief summary of the indications and contraindications to the use of procaine intravenously is to appear soon in POSTGRADUATE MEDICINE.

The indications fall generally into six main groups: (1) allergic states (serum and drug reactions); (2) pruritus (jaundice, some dermatoses, etc.); (3) pain (postoperative, traumatic, burns); (4) vasospastic disorders (causalgias, thrombophlebitis, arteritis, etc.); (5) bronchospasm, and (6) anesthesia where complete relaxation is not required.

Fair to good results have also been reported in the treatment of: osteoarthritis, acute rheumatoid arthritis, other diseases where muscle spasm plays a role, cardiac arrhythmias, acute anuria, cerebral manifestations of carbon monoxide poisoning, tinnitus aurium, and a variety of other conditions related to the above. It is apparently of little value in treating pain due to neuritis or direct nerve pressure.

Intravenous procaine is contraindicated only in the apparently *rare* cases of proved idiosyncrasy to procaine. However, deaths have been reported following its use. Arteriosclerosis and angina pectoris are not contraindications; indeed the drug has proved effective in angina pectoris decubitus, replacing morphine and nitroglycerin.

Toxicity occurs only on very rapid injection of excessive amounts of procaine and may be due to simultaneous administration of epinephrine. However, epinephrine has been used in treating anaphylactic reactions thought to be due to procaine. Toxic symptoms vary with the individual and include: tremors, convulsions, arrhythmias, apprehension, faintness, hypotension, and vomiting. These may be prevented by premedication with barbiturates and administration with glucose and ascorbic acid.

There are no known references on the use of intravenous procaine in the treatment of migraine-like headaches but the rationale might be the same as for the use of antihistaminics or vasodilators. A trial course of daily injections of 500 cc. of 0.1 or 0.2 per cent procaine in glucose with 500 mg. of ascorbic acid might be of benefit during one of the episodes. The periodicity in a 52-year-old woman suggests that estrogens might also be tried.

ROBERT M. KERR

NORMAL SEDIMENTATION RATE UNUSUAL IN RHEUMATIC FEVER

QUESTION: I would like to have your opinion on the interpretation of a sedimentation rate (Westegren) with an absolutely negative reading, i.e., 0 mm. at the end of one hour. In twenty-four hours there was only a drop of 3 mm. This was not due to faulty technic.

The patient in question shows pronounced symptoms of rheumatic fever. He is 21 years old, pulse 160, temperature 99° F., marked swelling of left knee and ankle, and evidence of heart changes is shown on chest x-ray and electrocardiograph.

To complete the picture the sedimentation rate should be increased. Does this negative reading have any significance? What conditions would cause a minus reading?

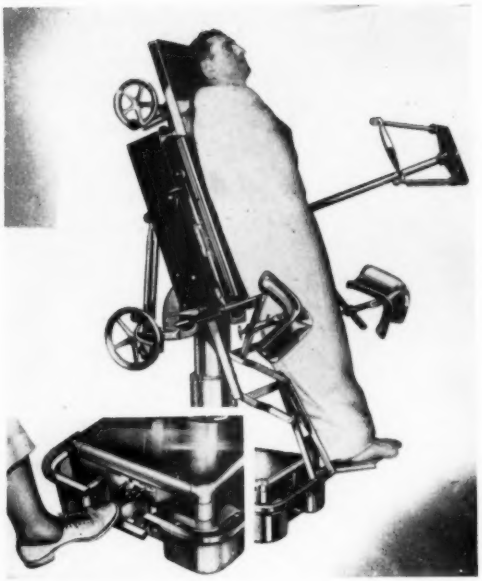
M.D.—North Dakota

ANSWER: It is quite unusual to have a normal sedimentation rate when the patient has definite evidence of active rheumatic fever. The symptoms described and the normal sedimentation rate strongly suggest the possibility of undulant fever. This should definitely be ruled out in this case.

M. J. SHAPIRO

New Drugs *and* Instruments

Information published in this department has been supplied by the manufacturers of the products described.



SISK UROLOGICAL X-RAY TABLE

DESCRIPTION: Foot lever on table activates an electric motor which controls the height of the table hydraulically—between 32 and 47 inches. The 1/3 H.P. electric motor, micro-switch, and all electrical connections and cord meet the requirements of the Underwriters' Laboratories for use in Class 1, Group C locations. Table has full 90° rotation in the vertical plane, adjustable back rest, stainless drain pan, retractable foot rest, and scientifically designed knee crutches. Base is welded steel, coated with stainless steel.

PRODUCER: Ohio Chemical and Surgical Equipment Co., Madison, Wis.

HEPCOVITE

PURPOSE: Solution of vitamin B_{12} for intramuscular injection.

INDICATIONS FOR USE: Pernicious anemia (uncomplicated or with neurologic complications), nutritional macrocytic anemia due to vitamin B_{12} deficiency, tropical and nontropical sprue, and certain other cases of macrocytic anemia.

HOW SUPPLIED: 10 cc. multiple dose vials or 1 cc. ampules—15 micrograms per cc.; also in 5 cc. multiple dose vials—30 micrograms per cc.

PRODUCER: Endo Products, Inc., Richmond Hill, N. Y.

PROCAINE PENICILLIN-G AQUEOUS SUSPENSION

PURPOSE: Intramuscular penicillin therapy.

COMPOSITION: Each cubic centimeter of aqueous suspension contains 300,000 units of the procaine salt of penicillin-G consisting of one molecule of penicillin-G combined with one molecule of procaine base.

DOSAGE AND ADMINISTRATION: Before injection, aspirate to make certain needle has not entered a vessel. When multiple injections are required, different sites should be selected. A single injection of 1 cc. will, in most patients, provide blood levels well above minimum therapeutic requirements for twenty-four hours or longer.

CAUTION: *Use only by intramuscular injection.*

HOW SUPPLIED: In 10 cc. multiple dose vials, boxes of 1 vial.

PRODUCER: Schering Corporation, Bloomfield, N. J.

METHERGINE

PURPOSE: To prevent excessive blood loss following delivery, to arrest secondary puerperal hemorrhage, to hasten involution of the uterus following delivery.

COMPOSITION: Methergine is methylergonovine, the first ergot alkaloid to be prepared by chemical synthesis.

DESCRIPTION: Has a highly selective uterotonic action, rapidly inducing strong uterine contractions following either oral or parenteral administration.

CAUTIONS: Should not be used during pregnancy, and should be administered with caution in patients with sepsis or impaired renal or hepatic function. It is of lower toxicity than other ergot alkaloids.

DOSAGE AND ADMINISTRATION: *Parenteral:* 1 cc. intravenously or intramuscularly to prevent postpartum hemorrhage; if necessary, dosage of ½ to 1 cc. can be repeated after two to four hours. *Oral:* One tablet (0.25 mg.) two to four times daily to hasten involution of the uterus.

HOW SUPPLIED: 1 cc. ampules containing 0.2 mg. methylergonovine, and tablets containing 0.25 mg. methylergonovine.

PRODUCER: Sandoz Pharmaceuticals, New York, N. Y.

DODEX (WITH ORAL ACTIVATOR) TABLETS

PURPOSE: Anti-anemia preparation.

COMPOSITION: Each tablet contains 2 micrograms of vitamin B_{12}, with 200 mg. of a natural pyloric substance.

DOSAGE AND ADMINISTRATION: About 5 Dodex tablets per day will suffice in most cases, although dosage must be adjusted to individual case.

HOW SUPPLIED: Bottles of 100 and 1,000 tablets.

PRODUCER: Organon, Inc., Orange, N. J.

UROKON SODIUM 30%

PURPOSE: Contrast medium for urography.
COMPOSITION: Urokon sodium is sodium 3-acetylamino-2, 4, 6-triiodobenzoate, a stable organic iodine compound, occurring as a white, crystalline powder, freely soluble in water. Furnished as a 30 per cent (w/v) sterile aqueous solution, it has an iodine content of 65.8 per cent.
HOW SUPPLIED: In 25 cc. ampules, boxes of 1, 5 and 20.
PRODUCER: Mallinckrodt Chemical Works, St. Louis, Missouri.

LIPOGEST

PURPOSE: Lipotropic agent.
COMPOSITION: Contains choline dihydrogen citrate 220 mg., dl-methionine 85 mg., and inositol 43 mg.
INDICATIONS FOR USE: In cirrhosis and related hepatic disorders.
HOW SUPPLIED: Bottles of 100, 500, and 1,000 capsules.
PRODUCER: George A. Breon & Co., Kansas City, Mo.

ZYOCEL TABLETS

PURPOSE: Regulative therapy in constipation.
COMPOSITION: Each tablet contains:

Methylcellulose, 400 cps.	0.5 gm.
Thiamine hydrochloride	2.0 mg.

DOSAGE AND ADMINISTRATION: Initially, 3 tablets with glass of water, three or four times daily until relief is obtained (usually three or four days). A maintenance dose of 1 tablet, three times daily, should be satisfactory. Adequate water intake is essential.
HOW SUPPLIED: Bottles of 50 and 100.
PRODUCER: Reed & Carnrick, Jersey City, N. J.

MAXISERVICE

PURPOSE: Comprehensive x-ray service plan providing equipment, tubes, instruction, and maintenance.
DESCRIPTION: For one monthly fee, this service plan provides the specific equipment to meet the physician's x-ray requirements. All inspection, repair service, installation, maintenance service, technical instruction and tube replacements are included. Covered by Maxiservice are the Maxicon, the Maxiscope, Photo-Roentgen units, the Maximar 100, the Maximar 250-III, and the Maximar 400. Complete information available from:
PRODUCER: General Electric X-Ray Corporation, 4855 Electric Ave., Milwaukee 14, Wis.

BENAT WITH B_{12} (ORAL)

PURPOSE: Treatment of retarded growth in children and general nutritional deficiencies of the vitamin B complex.
COMPOSITION: Each tablet contains:

Whole liver concentrate (1:24)	100 mg.
containing a minimum of vitamin B_{12} activity	1 microgram
Vitamin B_{12} concentrate, equivalent to	4 micrograms
Total vitamin B_{12}	5 micrograms
Thiamine mononitrate (B_1)	5 mg.
Riboflavin (B_2)	2 mg.
Niacinamide	50 mg.
Calcium pantothenate	5 mg.
Pyridoxine hydrochloride (B_6)	1 mg.

DOSAGE AND ADMINISTRATION: Average adult dose: prophylactically, 1 or 2 tablets daily; therapeutically, 2 to 6 tablets daily. Children according to age.
HOW SUPPLIED: Bottles of 24 and 100 tablets.
PRODUCER: The National Drug Company, Philadelphia, Pennsylvania.

LIPOCAPS

PURPOSE: Lipotropic therapy.
COMPOSITION: Each capsule contains:

Choline bitartrate	450 mg.
dl-Methionine	150 mg.
Inositol	100 mg.

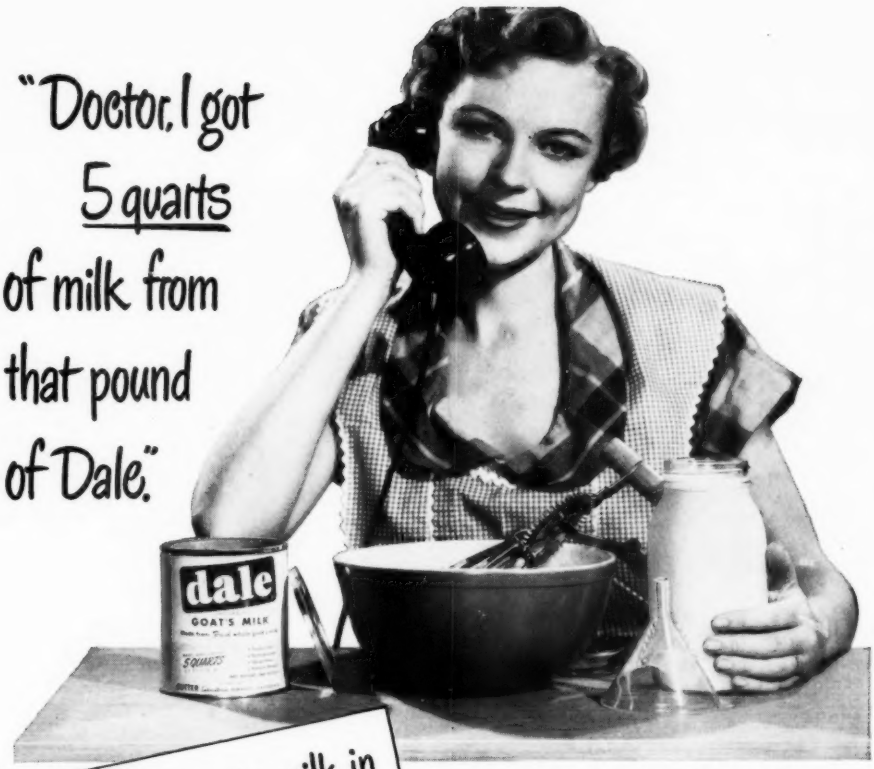
INDICATIONS FOR USE: In cirrhosis and other liver disorders, diabetes, atherosclerosis, infertility and disturbed fat metabolism.
HOW SUPPLIED: Bottles of 100 capsules.
PRODUCER: Lakeside Laboratories, Inc., Milwaukee, Wis.

CALADRYL LOTION

DESCRIPTION: Light flesh colored, slightly perfumed pharmaceutical preparation containing 1 per cent of Benadryl hydrochloride in a calamine-lotion type vehicle, with camphor and glycerin.
INDICATIONS FOR USE: In combating many types of itching and burning sensations experienced during the summer, such as those caused by sunburn, windburn, hives, poison ivy, poison oak, insect bites, and other minor skin irritations.
HOW SUPPLIED: In 6-ounce bottles.
PRODUCER: Parke, Davis & Company, Detroit, Mich.

(Continued on page A-50)

"Doctor, I got 5 quarts of milk from that pound of Dale."



dale is goats milk in its most economical form!

Dale Dehydrated Goat's Milk solves both doctors' and patients' problems when goat's milk is indicated in the diet. It is convenient, safe, dependable, scientifically uniform goat's milk in its most *economical* form.

EASY TO USE. Simply by adding cold or warm water Dale quickly mixes into a delicious fluid milk, recapturing its original freshness without tasting "canned". Requires no refrigeration.

SAVES TIME AND MONEY. It is 100% usable. Ounce for ounce, reconstituted Dale is as economical as *any* form of goat's milk. There is no loss from adherence to the can or from spilling or souring.

1 LB. EQUALS 5 QUARTS. One pound of Dale Dehydrated Goat's Milk, when reconstituted, makes approximately 5 quarts of whole fluid milk *as needed*. Dale is scientifically uniform.

PLEASANT TASTE. "Goaty" flavor and odor eliminated by the dehydration process —without any loss of healthful food values.

Dale Dehydrated Goat's Milk is prepared from clean, fresh, whole milk obtained from selected herds maintained under rigid sanitary conditions. It is pasteurized, spray-dried and vacuum packed—providing a reliable year-round source of whole, pasteurized goat's milk. In 8 oz. and 1 lb. cans. Descriptive folder available upon request—write Dept. H-35 Cutter Laboratories, Berkeley, California.

in cases of allergy
for special diets
when mother's milk
is unavailable

Specify dale DEHYDRATED GOAT'S MILK

available in drug stores

Distributed by **CUTTER LABORATORIES** · BERKELEY, CALIFORNIA

GUTTA TEST

PURPOSE: Complete routine chemical analysis of urine in one minute.

DESCRIPTION: Technic is as follows: (1) clean spot-plate and urine dropper thoroughly; (2) place a drop of reagent 1 in the first concavity, a drop of reagent 2 in the second concavity, continuing until the seven reagents have been placed; (3) one drop of urine is next added to each of the reagents; (4) rotate the spot-plate gently to blend the reagent and urine; time reaction from this moment; (5) read the results. Reagents are timed to show accurate readings at exactly one minute after blending. A positive reaction occurring after one minute should be disregarded. Tests for *p*H, albumin, sugar, acetone, indican, bile, and occult blood are interpreted by comparing with the colorimetric check chart on the box.

CAUTION: Some of the reagents are corrosive; others will stain clothing or hands. Therefore, ordinary care should be taken not to spill the reagents.

HOW SUPPLIED: Complete test set (300 tests), including 7 reagents, color chart, spot-plate, urine dropper, all packed in a permanent container. Reagent refills in dropper bottles also available.

PRODUCER: Biochemical Methods, Inc., Hollywood, Calif.

ACID-V CAPSULES

PURPOSE: Vitamin supplement for the diet of adult patients with hypochlorhydria and achlorhydria.

COMPOSITION: Each capsule contains:

Glutamic acid hydrochloride	300 mg.
Thiamine hydrochloride (vitamin B_1)	2 mg.
Riboflavin (vitamin B_2)	1 mg.
Niacinamide	10 mg.

DESCRIPTION: Designed to disintegrate in the stomach, releasing glutamic acid hydrochloride that furnishes hydrochloric acid, thus aiding in the absorption of the B vitamins.

DOSAGE AND ADMINISTRATION: Recommended dosage is one capsule three times daily.

HOW SUPPLIED: Bottles of 100 and 1,000.

PRODUCER: Sharp & Dohme, Inc., Philadelphia, Pa.

PAR-PEN

SMITH, KLINE & FRENCH LABORATORIES, Philadelphia, have made two major changes in Par-Pen—for use in displacement therapy of sinusitis: (1) strength increased to 5,000 units of penicillin per cubic centimeter; (2) package size now a ½ fl. oz. (15 cc.) bottle. When dispensed as directed, the new Par-Pen will contain for one week, at room temperature (not above 75° F.), not less than 5,000 units of crystalline potassium penicillin G, and 1 per cent Paredrine hydrobromide.

DIODRAST CONCENTRATED AQUEOUS SOLUTION 70%

PURPOSE: Angiocardiography in infants and children.

DESCRIPTION: A 70 per cent aqueous solution (by weight/volume) of Diodrast, the diethanolamine salt of 3,5diiodo-4-pyridone-N-acetic acid which contains 49.8 per cent of iodine. Each 20 cc. ampule contains 14 gm. of Diodrast.

INDICATIONS FOR USE: Satisfactory visualization in infants and children has been obtained by using 1 cc. of the solution per kilogram of body weight and slightly smaller amounts in older children.

DOSAGE AND ADMINISTRATION: Detailed directions in package circular.

HOW SUPPLIED: Ampules of 20 cc. containing 14 gm. of Diodrast, and ampules of 50 cc. containing 35 gm. of Diodrast.

PRODUCER: Winthrop-Stearns, Inc., New York, N. Y.

THERAPEUTIC FORMULA VITAMINS

PURPOSE: For patients who require multivitamin therapy, but for whom physicians feel administration of folic acid is unnecessary.

COMPOSITION: Each capsule contains:

Vitamin A	25,000 U.S.P. units
Vitamin D	1,000 U.S.P. units
Thiamine hydrochloride (B_1)	10 mg.
Riboflavin (B_2)	5 mg.
Niacinamide	150 mg.
Ascorbic acid (C)	150 mg.

INDICATIONS FOR USE: Before or following surgery; in convalescence; in nutritional failure of the aged; cases of prolonged illness; and for severe vitamin deficiencies.

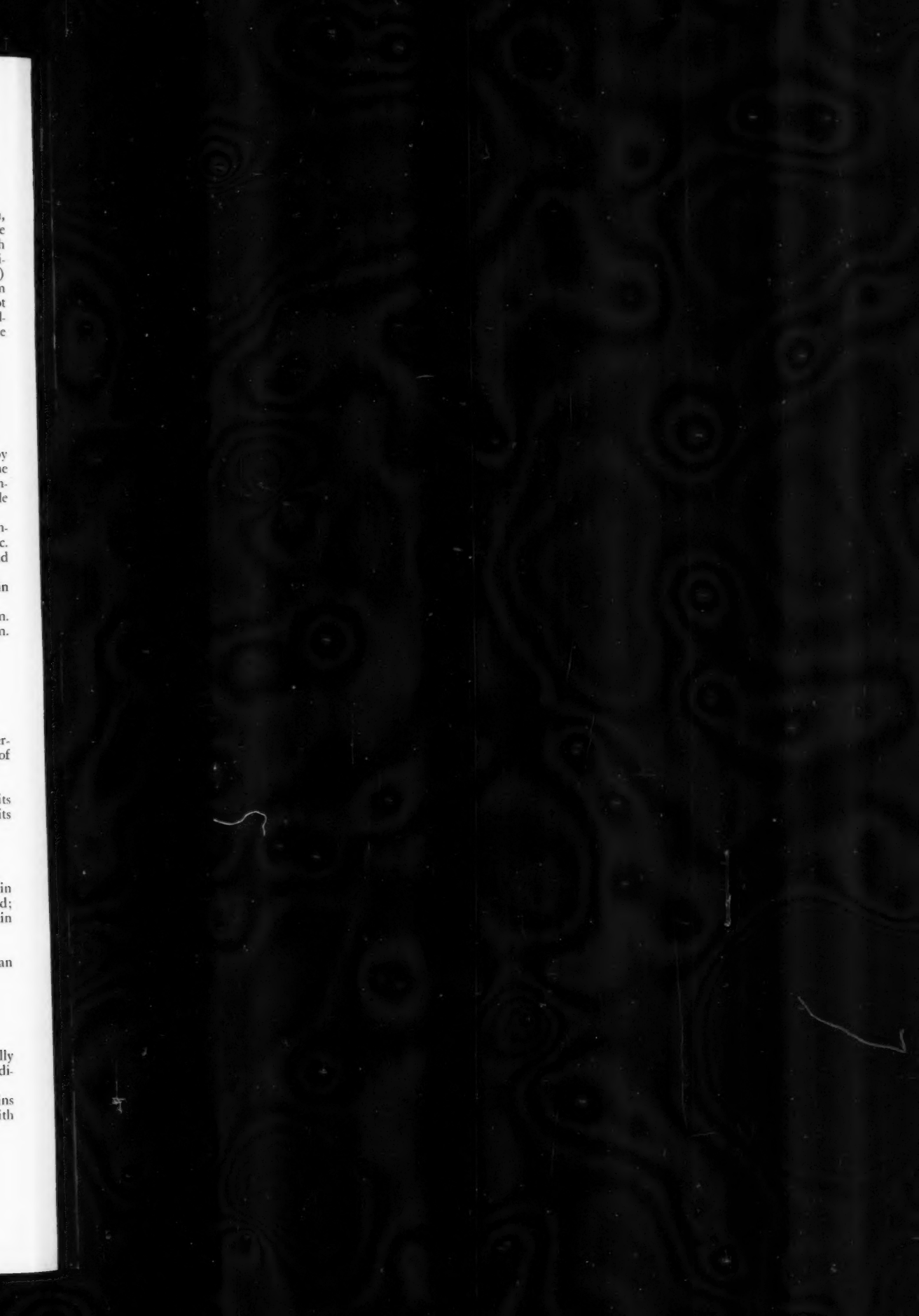
HOW SUPPLIED: Bottles of 30, 100, 250, and 1,000.

PRODUCER: Lederle Laboratories Division, American Cyanamid Co., Pearl River, N. Y.

DULCET PENICILLIN TABLETS

PURPOSE: Oral penicillin therapy. Designed especially for children, and for adults who dislike taking ordinary tablets.

COMPOSITION: Each green, mint-flavored cube contains 100,000 units crystalline penicillin G potassium with 0.25 gm. calcium carbonate as a buffer.

HOW SUPPLIED: Bottles of 12 and 100 tablets.

PRODUCER: Abbott Laboratories, North Chicago, Ill.